American Heart Journal

VOL. 29 FEBRUARY, 1945 NO. 2

Original Communications

CLINICAL AND THEORETICAL CONSIDERATIONS OF INVOLVEMENT OF THE LEFT SIDE OF THE HEART WITH ECHINOCOCCAL CYSTS

A REVIEW OF THE LITERATURE, WITH A REPORT OF FIVE NEW CASES, INCLUDING ONE OBSERVED BY THE AUTHORS

JOHN H. PETERS, M.D., LEWIS DEXTER, M.D., AND SOMA WEISS,† M.D.
BOSTON, MASS.

ECHINOCOCCAL disease holds a somewhat unique position in that, despite the fact that it is extremely common in some areas, it has been given close attention by a surprisingly small number of investigators. The early work on pathologic anatomy and life cycle was thorough. Although some doubt exists regarding the actual mode of transmission from animals to man,[1] hypotheses have been advanced which seem tenable in the absence of direct proof.[2, 3] Studies of the disease in man have been limited principally to case studies, statistical compilations, reviews of surgical techniques, and pathologic reports. Transmission, pathogenesis, and the mechanism of human infestation, all factors of vital importance in the understanding of any disease, have been left as the province of a small group of men in various endemic areas, and it is to them that we owe our present knowledge.

Clinical echinococcosis is predominantly a hepatic and pulmonary disease. Its surgical therapy has been extensively discussed in the world literature. This paper is concerned with the small group of cases in which the primary infection passes through the hepatic and pulmonary filters to involve the heart, and secondarily the peripheral organs. Although such cases constitute, at most, less than 2.5 per cent of total human infestations with the dog tapeworm,[4, 5] they are important and interesting to the clinician because of the challenge they present in terms of diagnosis and treatment.

From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

Received for publication April 3, 1944.

†Deceased.

The contemporary literature of this disease suffers from the fact that many of those who have concerned themselves with the theoretical aspects of human echinococcosis have published their observations in the foreign literature, so that much of the material is not readily available. That this is particularly true of the cardiac type of infestation is due, first, to the rarity of the condition, and, second, to the fact that it is an affliction which had only once been suspected ante mortem prior to 1905,[6] and only once definitely diagnosed before 1925.[7]

Professor F. Dévé, of France, is the figure who stands out as the authority on echinococcal disease. There is no entirely adequate summary of his work on cardiac echinococcosis in English, and much of his writing is not easily obtainable. Thus it seems wise at this time to allow the diagnosis of a case of cardiac echinococcosis to serve as the basis for a discussion of the subject. Arce's papers[2] on hydatidosis have recently offered an excellent background for the study of the more common forms of the disease.

In our analysis of the literature we have collected fifty-six of the at least seventy-five reported cases of cysts of the left side of the heart. To these we have added five cases not previously reported, including one seen by the authors at the Peter Bent Brigham Hospital in the terminal phases (Case 1).

The cases cited in this paper do not constitute all of those in the literature for two reasons, namely, the inaccessibility of certain of the articles, and the unsuitability of some of the reports for proper analysis. It has been necessary to be somewhat arbitrary in deciding whether or not to include certain cases of involvement of the cardiac septa in this series. An effort was made to include only those cases in which the left side of the heart was definitely infested.

History.—Prior to 1900, cardiac echinococcosis could be studied in the literature in numerous post-mortem reports and tabulations of such reports,[8-16] but from little else. It is true that some of those charged with the care and examination of the victims of the affliction had ventured to speculate upon the origin of the cardiac cysts and the nature of the terminal events,[6, 17] but such studies were not productive of anything more than speculation. Therefore, when Dévé, of Rouen, first as a medical student and later as a professor, began his investigations into the mechanism of echinococcal disease, particularly of possible routes of infestation and of the dissemination of the parasite within the body, he found himself working in an almost virgin field. He and his pupils remain the authors of virtually all definitive work on this disease.

The first report of cystic disease of the heart which is definitely identifiable as echinococcal dates from 1836.[18] Until the time of Dévé's thesis,[19] in 1901, the number of cases of primary involvement of the left side of the heart and the systemic circulation numbered at least thirty-five. Since then this number has been augmented by about forty more.

It was early noted that the condition of these cysts of the heart varied. Originally reported as incidental autopsy observations, cases began to appear in which the rupture of cysts had obviously caused death.[8, 20, 21]

It had always been recognized that the liver was the most common site of echinococcal cysts, followed by the lungs, and that the peripheral organs were far less frequently involved. It remained for Dévé, in the early years of this century,[4, 19, 22-28] to explain the mechanisms responsible for this distribution. In 1887 a cardiac cyst was first suspected as the cause of illness prior to death,[6] but it was not until the roentgen ray came into use that the first definite ante-mortem diagnosis was made (1905[7]). Since that time, additional ante-mortem diagnoses have been reported, including one[3] in North America.

The possibility of operative removal of such cysts was suggested early, but the earliest reported attempt at such therapy that we have found was in 1921,[29] and the first successful operation was reported in 1932.[30] Removal of a peripheral embolus arising from rupture of a cardiac cyst had been reported in 1889.[13]

Since the total number of cases in which the disease was diagnosed and treated remains so small (six and two cases, respectively) it must be obvious that the history of this condition remains largely unwritten, and that evaluation of the use of newer skills in thoracic surgery will be impossible for some time to come.

Occurrence.—The geographic occurrence of hydatid disease of the heart is, as one would expect, that of echinococcosis in general. Australia, New Zealand, North Africa, Europe, Asia Minor, Argentina, and Uruguay are the areas where it originates. A certain number of North American cases have been reported, although most of these persons incurred their original infestation in foreign parts.[31, 32] Of recent years several cases have been reported in natives of this continent,[3, 32, 33] and the question has arisen as to their origin. The appearance of such cases has reflected an increase in the extent of infestation of native cattle[33-35] (Table I). Curiously enough, the source of human infestation does not seem to be dogs, as it is in most endemic areas.[35, 36] This has led some to think that the American reservoir may be in wild animals,[37] which would render the problem of control far more difficult than in areas such as Iceland, where the disease has all but been wiped out by intelligent control measures,[38] and New Zealand, where attempts are be-

TABLE I

INCIDENCE OF ECHINOCOCCUS INFESTATION IN CATTLE AND CALVES IN THE UNITED STATES*

YEARS	NUMBER OF CATTLE EXAMINED	NUMBER OF CATTLE WITH HYDATIDS	REFERENCE
1897 to 1899	8,831,927	6	35
1937	17,314,451	1,923	34
1941	15,520,427	3,525	34

*Figures for sheep and pigs not available for recent years, but rate of infection higher than in cattle in 1897 to 1899.[35]

ing made to do so with less success.[39] The increase in the number of diagnosed hydatids in North Americans has led Magath[33] to the belief that the disease is becoming, or has become, endemic in man in this country.

There is a definite relation of cardiac infestation to age. Dévé[25, 28] pointed out, as have others,[40, 41] that it is probable that the original infestation in human beings occurs usually in children, but that its clinical manifestations do not appear with great frequency until considerably later (except in the case of intracranial cysts) because they must attain sufficient size to cause mechanical interference with the affected organ before making themselves known. Cardiac cysts have only rarely given rise to symptoms before the age of 20 years, and the most common age for discovery is in the third and fourth decades, excepting that group of cases in which symptoms never develop and cardiac cysts are found incidentally at autopsy. Reports have been published, however, of cysts at all ages from 11 to 70 years.

The location of cardiac cysts is governed by the anatomy of the coronary arteries.[19] Because the entrance of the right coronary is more direct than that of the left, the majority of cysts are found in the right side of the heart, roughly in the proportion of 3:2.[17, 18] Since the incidence of cardiac cysts has been estimated at 0.5 to 2 per cent of all echinococcal cysts,[4, 5] the cases of involvement of the left side of the heart constitute, at most, 0.75 per cent, and more probably less than 0.5 per cent, of all cases.

The auricles are far less often affected than the ventricles.[40]

The difference between the sexes in the incidence of the disease is the same as in all echinococcal disease, with males predominating;[40] the ratio is about 2:1,[33, 40, 41] presumably because of occupational exposure.

Etiology and Pathogenesis.—The primary form of the organism is the dog tapeworm, *Echinococcus granulosus.* Dogs are infested by eating uncooked cysts, and therefore the disease predominates in stock-raising areas, particularly in sheep-grazing regions where dogs are kept for tending sheep. Magath[42] has pointed out that in America and England, where the tradition has been maintained that sheep dogs must never be allowed to feed on mutton, the disease has never flourished, whereas formerly in Iceland,[38] and at present in Australia, New Zealand, and Argentina, where such dogs are fed on uncooked offal from sheep and cattle, canine infestation and human disease are widespread.[33, 41]

The mode of transmission of the larvae from the dog intestine to human beings remains in some doubt.[1] In animals this takes place as a result of pollution of grazing grounds by dogs. Since some 70 per cent of human cysts are hepatic, it is presumed that the larvae travel by way of the digestive tract, but definite proof is difficult, if not impossible, to obtain. Dévé has suggested[25] that infestation takes place almost entirely in childhood, when association with pets tends to be most intimate,

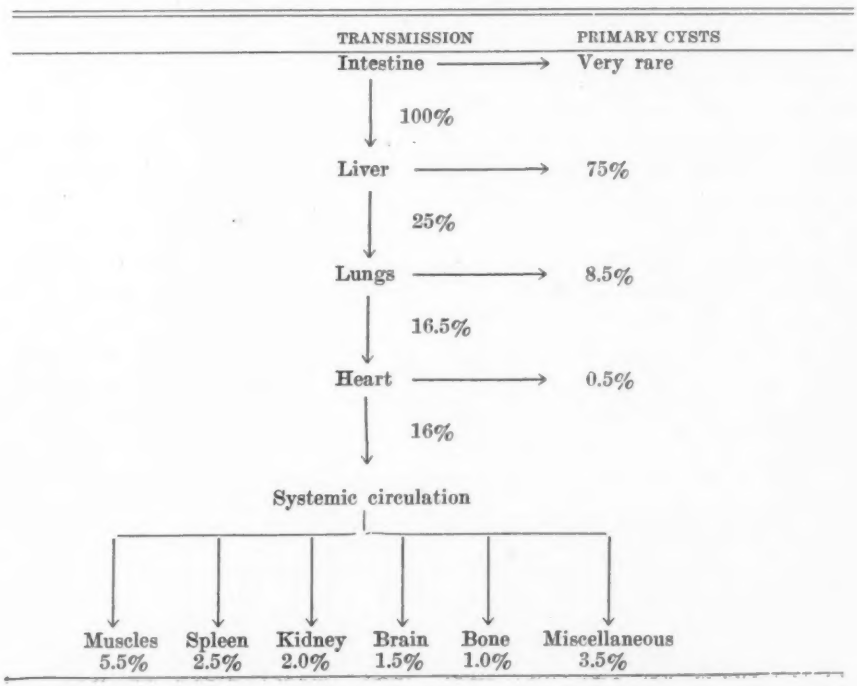
and Dew[41] and Magath[33] are of the same opinion. The most telling point in Dévé's argument is that one virtually never sees primary intracranial cysts except in childhood.[43, 44] Elsewhere in the body the cysts can develop and grow asymptomatically for long periods, and are frequently not diagnosed until patients are older, whereas, in the cranial vault, such expansion cannot proceed indefinitely.

After leaving the digestive tract the larvae enter the portal circulation and are largely filtered out by the liver, where an unknown and probably variable proportion survive to form cysts. A far smaller number of larvae pass the liver filter and enter the heart and pulmonary tree, where about a third of them are retained in the capillary bed, and the remainder pass into the systemic circulation. Dévé[4] has suggested that the reason why the pulmonary filter is less effective than the hepatic is that the liver removes all of the larger larvae and that the pulmonary capillaries are relatively large. The eventual distribution of primary cysts is illustrated in Table II.

These primary cysts, contracted presumably in childhood, do not interest us further aside from the small percentage which are retained by the heart, except insofar as we are interested in differentiating them from secondary cysts arising from primary cardiac cysts. The cardiac cysts are formed by the entrance of the larvae into the coronary system.[19]

TABLE II

ROUTES OF INFESTATION AND SITE OF PRIMARY ECHINOCOCCAL CYSTS IN MAN—AFTER DÉVÉ[4]



The anatomy of the coronary arteries is such that the larvae are most easily carried directly into the right coronary, and, as a result, the proportion of cysts is roughly 3:2 for the right and left sides of the heart, respectively.[17, 28]

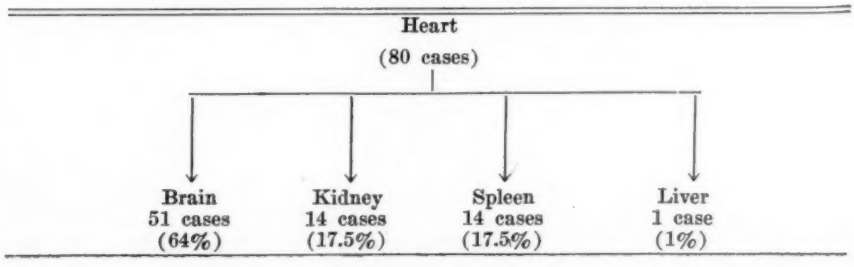
The cysts may develop in several ways. A certain proportion of them die after attaining varying sizes, after which, unless they are so placed or so large as to cause mechanical difficulties, they become fibrosed, with or without calcification, and are only discovered incidentally at operation or autopsy. Living cysts grow at what seems to be a fairly constant rate, depending on their location, and, from their size, much may be inferred regarding their age. A certain proportion of cysts rupture as a result of trauma or interference with blood supply and necrosis. When this occurs, spread of the disease frequently follows by any one of a number of routes. There may be merely local formation of multiple cysts in the tissues immediately surrounding the site of rupture, but if the rupture is into the peritoneal cavity, large blood vessels, biliary passages, or respiratory or digestive passages, distant spread will usually take place unless the cyst is dead, or unless the infesting material can be completely expelled in bile, feces, sputum, or vomitus. This infesting material may consist simply of cyst fluid and scolices, or it may contain actual "daughter cysts" formed by infoldings of germinal membrane following trauma to the cyst.[27] These daughter cysts have the capacity of independent growth when carried elsewhere in the body by the blood stream or in other ways. Table III depicts the routes of spread from rupture of primary cardiac cysts to various organs.

There are five main types of cardiac cysts, as follows: (1) dead cysts, usually markedly fibrosed or calcified, (2) living, intact cysts, (3) cysts which have ruptured into the pericardium, causing adhesions, with or without the formation of secondary cardiac cysts, (4) pedicled cysts in the heart cavities, and (5) cysts which have ruptured one or more times into the chambers of the heart.

The division of cardiac cysts into the above five groups is of importance because the clinical picture is governed by the location and viability of the cyst.

TABLE III

SITE OF EMBOLI FROM CYSTS OF THE HEART—FROM DUMONT[40]



The first group is one which is least frequently of clinical significance. As a rule such cysts are found only at autopsy, and do not cause symptoms except when death of the cyst is preceded by rupture, with dissemination of viable echinococcal material. They may, however, be of such size or so located as to interfere with the function or circulation of the heart.

The living, intact cysts are perhaps the most important of the entire group, for, if they are detected roentgenologically, the indication is for surgical exploration and extirpation to prevent subsequent rupture or further growth, which may interfere with cardiac function.

Pericardial involvement, with its complications, may be an indication for surgical intervention, although the potential dangers and technical difficulties of such operations may be prohibitive. Dévé[24] has pointed out that it is rupture inwards, rather than outwards, which causes most trouble from cardiac cysts.

Pedicled cysts in the chambers of the heart are found from time to time post mortem. Occasionally they cause symptoms if they are so large or so placed as to interfere with valvular function. Their detection is unlikely, although the possibility was considered ante mortem in one case.[6] Under such circumstances operative intervention might be conceivable, but differentiation from other valvular lesions would be difficult.

The detectable cysts are probably largely contained in the fifth group. Group two may be detected in routine chest roentgenograms, and since such examinations are becoming a more and more common practice, this will undoubtedly happen more frequently than in the past. However, since such cysts are frequently asymptomatic, they will not be found by other means in significant numbers. When cyst contents are poured into the systemic circulation, however, symptoms almost always result. It is at the time of rupture, therefore, that most ante-mortem diagnoses should be made. This will be most often true of cysts which pour daughter cysts into the vascular tree.

When such a cyst ruptures, several systemic disturbances are to be anticipated. The first cause of such disturbances is mechanical, that is, the result of arterial occlusion by daughter cysts and other material, e.g., cyst wall, scolices, etc. It is of interest in this regard that when such material occludes arteries and causes symptoms, it is usually a large artery that is involved, e.g., femoral, iliac, carotid, or renal. This is probably due to the fact that involvement of smaller arteries is obscured by the general systemic and vascular reactions to be noted below.

A secondary effect of these emboli is the dissemination of germinal elements from the primary cyst into the peripheral tissues and organs; these may or may not survive and later give rise to secondary cysts with or without eventual clinical significance, depending on the survival of the patient and on the survival of the secondary implantations. Many of these die shortly after implantation, others survive to form cysts which

later die, and still others progress to give symptoms, may develop daughter cysts, and may even rupture themselves at a later date to cause further dissemination. If the particles forming emboli are quite large, they usually cause local ischemia about the infarcted area, with death of the cystic material, followed by scarring about the site of implantation.[40] The affected vessel may even recanalize after the death of the occluding cystic matter. Aside from the mechanical effects, there is no specific symptomatologic reaction to the implantation of germinal elements in the peripheral tissues.

Another important group of systemic disturbances is attributable to the reaction of the body tissues, particularly the vascular system, to the protein substances freed from the cyst at the time of rupture. The original invasion of the body by the cysts usually results in the development of sensitivity to echinococcal materials. However, as long as a cyst is intact in the body, the system is protected by the cyst membrane from exposure to such allergens. This sensitivity forms the basis for the numerous skin and serologic tests now in general use for the diagnosis of echinococcal infections.[42, 45-50] In this regard, it is of interest that patients with single cysts of the brain frequently fail to give a positive skin test, although the test may become positive after operative extirpation of such a cyst.[51]

When a cyst ruptures in the heart, freeing cyst contents in the peripheral blood stream, the reaction may be of any degree, depending on the viability of the cyst, and probably on other factors, such as duration of previous infestation, previous ruptures, and the like. As a rule, the effects of such a reaction constitute one of the principal components in the clinical picture.

A third important group of symptoms arises from the effect of the primary cysts on the function of the myocardium, either as a result of myocardial destruction, interference with valvular efficiency, or disturbance of conduction. Curiously enough, this type of disturbance does not figure prominently in the reported cases; it was noted in only thirteen of the fifty-six cases that we have reviewed.

Dévé[24] has pointed out that, in carefully followed cases, rupture of cysts into the pericardium is seldom fatal, and that rupture into the systemic circulation usually takes place several times before death occurs. Our case (Case 1) illustrates this, as do other case reports.[52-54] Were clinical data more fully described in other reported cases, this list would doubtless be longer.

Clinical Course.—Of the fifty-six cases of hydatid cysts of the left side of the heart that we have collected from the literature, fifteen, or 27 per cent, were discovered incidentally at autopsy.[10, 16, 17, 55-65] In these cases the cysts remained silent throughout life. Nine, or 16 per cent, of this group died suddenly, and an intact cyst constituted the only lesion at autopsy.[66-74] Although in this group there is some doubt as to whether or not the cyst was the cause of death, the relative fre-

quency of its occurrence suggests the sudden appearance of a fatal arrhythmia. Thirteen, or 23 per cent, had signs and symptoms of impaired cardiac function.[3, 6, 7, 14, 18, 29, 30, 68, 69, 71, 75-77]

In another group of cases the course was one of rupture of the cardiac cyst, with more or less prompt fatality, either due to anaphylaxis or to circulatory obstruction by cyst contents in the heart itself or in major peripheral vessels. In fourteen (25 per cent) of the fifty-six cases, rupture was the primary cause of death. Rupture, however, need not necessarily be followed by death. Our case (Case 1) is an example of repeated rupture into the heart, and, in sixteen (27 per cent) of the fifty-six cases, rupture had occurred previously without causing death. Without having ever seen a case, and at a time when adequate case reports were not yet available, Dévé wrote a prophetic description of what the clinical picture of rupture of a cardiac cyst into the systemic circulation would be, and subsequent observers of such cases have confirmed rather than corrected his predictions. His remarkable description follows (our translation); it is taken from a quotation by his pupil, Mlle. Dumont,[40] in her thesis on cardiac echinococcosis, written in 1918.

"Sudden onset in apparently totally healthy subject. Immediate onset of anxiety with or without lipothymic state or epileptiform crisis, or merely a sensation of tingling throughout the extremities. Headache with or without ocular disturbances. Often vomiting. Soon, pain in the extremities, accompanied by weakness or mild spasticity, accompanied particularly by circulatory disturbances of the extremities giving rise sometimes to ecchymotic areas or to marbling, sometimes to a true Raynaud's syndrome: cyanosis of the extremities, cold, decrease in intensity or disappearance of arterial pulsations, pain. Without doubt, one will often find, in such cases, a more or less profuse albuminuria, with or without hematuria, caused by microscopic renal emboli. Finally one can predict that an urticarial eruption may ensue to clarify the nature of these disturbances.

". . . such a description is entirely theoretical. Thus it makes no pretentions other than to state the problem and to call the attention of clinicians to a matter which has up to now remained obscure and which appears to us interesting. There is no doubt that, sooner or later, new clinical observations will fill the gaps (in our knowledge) and permit the substitution of a real symptomatology for our hypothetical estimate."

It is a real tribute to Professor Dévé that "substitution" of the "real symptomatology" is not necessary.

The patient's course subsequent to rupture of a cyst may take almost any form, depending upon the severity of the reaction to the echinococcal proteins, on the size and type of cyst ruptured, on the site and extent of embolic involvement, and on the degree of impairment of cardiac function resulting from interference with myocardial integrity. One of the most remarkable features of cardiac hydatids is the relative rarity

of disturbance of cardiac function by the cysts, even in cases in which the cysts are large and the continuity of the myocardium is definitely disrupted. This is in part explained by the nature of the encapsulating membrane, which serves in lieu of myocardium where it replaces it.

If the patient recovers from the initial shock of the rupture, he may be left with a gangrenous extremity, unilateral renal shut-down, hemiplegia, or other embolic sequelae; he may be entirely asymptomatic, only to be struck down by a subsequent recurrence or by the gradual development of multiple intracranial cysts, with epilepsy or other symptoms of intracranial growth;* or again the extension may be to other peripheral organs with corresponding symptoms.

It is not entirely justifiable to conclude that a cardiac cyst exists simply because of the sudden appearance of a shower of hydatid emboli in the peripheral circulation, because such cysts may originate from the rupture of pulmonary cysts into the pulmonary veins. This, however, is an occurrence which has only rarely been reported, for pulmonary cysts usually rupture into bronchial passages.

Diagnosis, Treatment, and Prognosis.—Of the fifty-six cases we have collected from the literature, in five,[3, 7, 29, 30, 51] or possibly six,[6] the diagnosis was made prior to death. In an additional case the diagnosis was made by Dr. H. R. Dew (Case 5 of this report). The diagnosis of cardiac echinococcosis is essentially the same as it is in the case of other organs of the body, with certain added difficulties which arise from the fact that heart cysts tend to be asymptomatic, and can, therefore, usually be detected only roentgenologically. There are a number of skin and serologic tests, none of which are universally satisfactory,[42, 45-50] although high specificity is reported for several—one as high as 85 to 95 per cent.[33]

Eosinophilia is reported in a considerable proportion of cases, although it is not always present, even after rupture of a cyst. The presence of one or more cysts in peripheral organs may serve as the clue which will lead to roentgenologic detection of a cardiac cyst. The sudden occurrence of unexplained anaphylactoid collapse, particularly in persons born in regions where hydatid disease is endemic, should always arouse suspicion of rupture of a cyst, particularly in the heart, for the freeing of echinococcal protein directly into the blood stream seems to cause such reactions in a greater proportion of cases than does the rupture of cysts elsewhere.

There is reason to believe on theoretical grounds that the presence of a cyst or cysts in the myocardium should give rise to abnormalities in the electrocardiogram, and a recent case in which tracings were obtained[3] bears this out. In our case (Case 1), the electrocardiogram was entirely normal except for minimal depression of the S-T segment in Lead IV.

*In this regard, Dévé's experimental production of intracranial pressure symptoms by the injection of scolices was probably the earliest and most satisfactory method for the study of increased intracranial pressure in the intact animal.[23]

Calcification of cyst walls, as seen roentgenologically, would appear to be a confirmatory, although not a specific, diagnostic point, for it is unusual for pulmonary cysts to show calcification.[3]

Treatment of cardiac cysts is a virtually virgin field. Long[30] reports a case in which operative removal of cyst contents in a 42-year-old woman was followed by recovery. Such treatment had been suggested in the past, but so far as we know this is the first case in which such treatment has been attempted. Recent advances in technique have rendered operations on the heart and pericardium far less uncommon than previously, and it may well be that operative removal prior to rupure will be the prophylactic therapy of choice in the near future. No other effective therapy is known, unless the physician in charge has sufficient temerity to attempt injection of the cysts after puncture and evacuation of the contents, which is unlikely with cardiac cysts. The one reported attempt[29] resulted in death. Aside from the one case noted, no attempts have apparently been made to treat such cysts up to the beginning of 1943. The evaluation of surgical measures, therefore, remains to be made in the future.

In deciding on operative treatment of cardiac cysts, two important factors should be given consideration. First, it should be ascertained whether or not the cyst has previously ruptured and caused extension, for the patient may benefit little from removal of a cardiac cyst if he is already being affected by secondary intracranial cysts. Secondary cysts elsewhere than in the brain can be dealt with later, but therapeutic success in dealing with multiple brain cysts is rare.[43] Second, one should attempt to differentiate cardiac cysts from pulmonary cysts adjacent to the heart, for the operative technique and prognosis are not identical (Case 6). Treatment should offer more if operation is undertaken prior to impairment of cardiac function by growth or intrapericardial rupture of the cyst.

It is well to point out the importance of accurate diagnosis with regard to intracranial cysts. Dew[43] has shown, as have others, that success in operative therapy of such cysts is dependent on elimination of cases of secondary involvement. Once a single primary cyst has been removed, recovery usually ensues if the patient survives the operation, but multiple secondary cysts can seldom be completely removed. A careful search for cardiac cysts, therefore, should always precede craniotomy in cases in which intracranial echinococcus cysts are suspected.

The prognosis of cysts of the heart should probably be considered unfavorable, although it is true that fifteen out of a total of fifty-six cardiac cysts were found incidentally at autopsy. Viable cysts must be expected to progress to the point of rupture or interference with cardiac function, and after the occurrence of either of the above the outlook must be considered ultimately fatal, although the patient may survive for a varying period. This may well be changed by operative treatment.

DISCUSSION

Echinococcal infestation of American cattle seems to be increasing, according to reports of slaughterhouse inspectors (Table I), and there is no reason to feel that the same is not true among our sheep and hogs, although figures are not available. This increase may well be reflected sooner or later by the appearance of cases of echinococcal infestation acquired in this country, although in the past almost all cases have been in foreign-born persons.[31, 32] Large numbers of American physicians are active at this time in areas where the disease is endemic (North Africa, Europe, Australia, and New Zealand), and there is every likelihood that they will encounter local inhabitants with this disease. Our own troops are not likely to become infested with echinococcus, however, because it is a disease which seems to be contracted predominantly in childhood. Transportation advances in the near future should bring physicians throughout the world into contact with a larger number of transient or permanent visitors from areas where this disease is common. Thus our physicians are more likely than before to be faced with the problems of echinococcosis.

Aside from the fact that such cases may be more frequently seen in the near future in North America, it is quite possible that advances in the technique of thoracic and cardiac surgery will offer cure, or at least relief, from a condition which previously had been of clinical interest but without therapeutic potentialities. Cardiac echinococcosis can profitably be added to the list of diseases of the heart which are amenable to surgical treatment.

SUMMARY AND CONCLUSIONS

Fifty-six cases of echinococcus infestation of the left side of the heart have been collected from the literature, and five new cases added. Invasion of the left side of the heart by echinococcus cysts has been discussed in detail from the point of view of pathogenesis, clinical course, diagnosis, prognosis, and treatment. Although this is a rare disorder, it is worthy of emphasis in that it represents a type of unusual heart disease for which surgical relief is promising, now that improved techniques of thoracic exploration have been developed.

REPORT OF CASES

CASE 1 (M59783).—M. D., a 43-year-old Italian housewife, was first seen at the Peter Bent Brigham Hospital on March 12, 1941, because of attacks of unconsciousness of nine years' duration. The family and past history were noncontributory except that she was born in Italy and came to this country in 1931. She had always been well until 1932, when she developed her first seizure. Her second attack occurred in 1937. Both attacks were similar, in that she was seized with sudden, sharp epigastric pain and loss of consciousness without aura. She became cyanotic, frothed at the mouth, and was found to be in profound shock; neither the blood pressure nor the pulse was obtainable. There were no

convulsions. She was incontinent of urine, and passed foul flatus which was colored by brick-red blood. No skin lesions were noted. With symptomatic treatment patient regained consciousness within a few hours and attained complete recovery within a week. A roentgenogram of the chest in 1937 showed no abnormality of the heart or lungs except for some thickening of the pleura at the right base laterally. Roentgenologically, the stomach, duodenum, and colon were likewise normal. The patient was asymptomatic for three years.

She developed seizures in April, 1940, February, 1941, and March, 1941. These attacks were preceded by sticking and "pinching" paresthesias of the lower half of the body, especially on the left, and by flashes of light. Flaccid unconsciousness, without convulsions, ensued, and lasted about thirty minutes. During the last attack the jaws were tightly clamped together and she drooled sputum. Black spots were said to have appeared on her left arm. During the period of recovery she had difficulty in swallowing and talking and weakness of the left arm and leg. At no time were cardiac symptoms apparent. A roentgenogram of the skull showed nothing abnormal. The blood sugar was 86 mg. per cent. The spinal fluid was entirely normal. An electroencephalogram was reported as "not typically epileptic, but abnormal."

On May 23, 1941, she had two mild attacks and was readmitted to the hospital because she was suspected of having a brain tumor. A roentgenogram of the chest at this time revealed two nodular masses, one opposite the ascending aorta on the right, and the other at the auriculoventricular junction on the left; they measured 4.5 cm. and 2.5 cm., respectively (Fig. 1). These masses could not be separated from the cardiovascular shadow and did not seem under the fluoroscope to have intrinsic pulsation. The mass on the left was described as apparently having the usual auriculoventricular junction motion. A ventriculogram on June 6, 1941, revealed moderate dilatation of both lateral ventricles and the third ventricle. More than the usual amount of air was around the Islands of Reil. The ventricles were displaced slightly to the right of the midline. The patient was discharged without a definite diagnosis.

She was readmitted Dec. 16, 1942, in coma. She had been well since discharge until the evening before admission, when at suppertime she suddenly felt ill. She lay down and was swept by the familiar sensation of pins and needles which were worse on the left side. She could hardly move that arm. Epigastric and lower abdominal pain and urinary incontinence ensued, but there was no loss of consciousness, aphasia, or convulsions. Her doctor found a temperature of 97° F., a pulse rate of 80, and a systolic pressure of 70 mm. Hg. She vomited on several occasions. Several hours later her face became swollen. Thick, tenacious material came from the mouth. She began to shake as if having a chill, and soon became unconscious. The next day her physician found her in coma and sent her to the Peter Bent Brigham Hospital.

Physical examination revealed a well-nourished patient in coma and breathing irregularly. Facial edema was noticeable. Many petechiae were observed over the chest, back, arms, and conjunctivae. The lips were dry. Rhonchi were heard throughout both lungs, and moist râles were heard at both bases. The heart sounds and rhythm were normal. The blood pressure was 84/66. Neither the brachial nor common carotid pulse could be felt on the right. The right arm was cooler than the left, but both legs were of the same temperature. Neither dorsalis pedis artery could be felt.

Neurologic examination revealed the following: The head was held to the left; the eyes were held in left conjugate deviation, with roving movements; the right pupil was larger than the left; there was questionable blurring of both nasal disc margins; a patch of exudate was seen in the left fundus, and one of the small arterioles was occluded; the jaws could not be opened. The arm reflexes were hyperactive, and rigidity was marked, especially on the left; the abdominal reflexes were not obtained; the leg reflexes were hyperactive, particularly on the left; Babinski, Oppenheim, and Gordon signs were present bilaterally; bilateral ankle clonus was noted, as well as fine muscular twitchings and urinary incontinence.

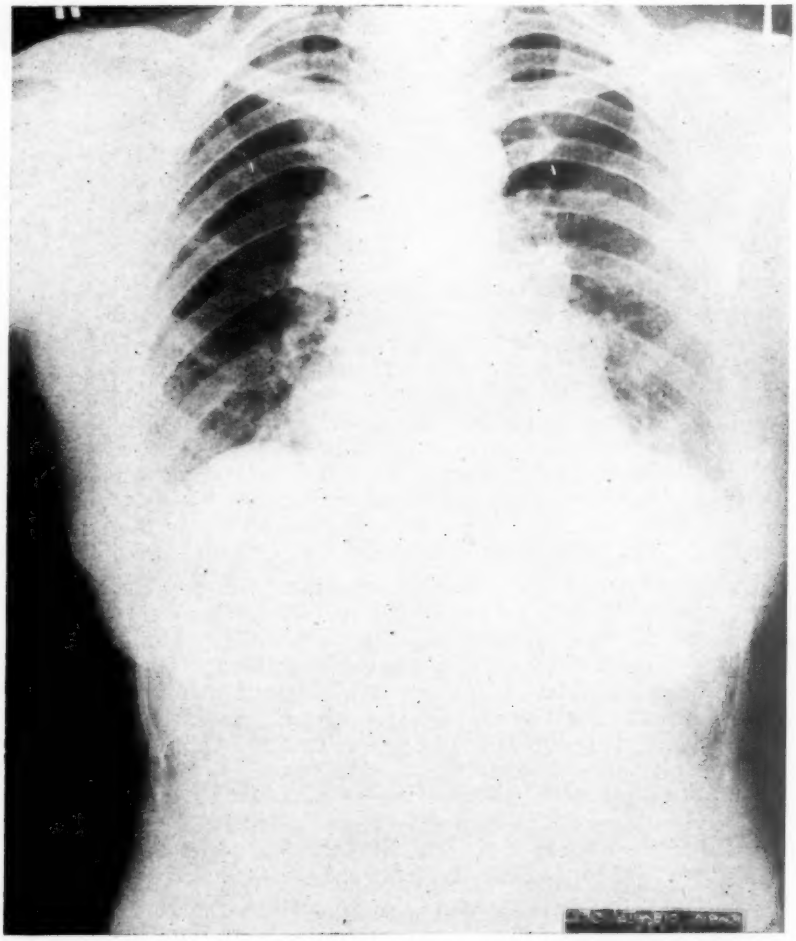


Fig. 1.—Roentgenogram of chest of patient M. D. (Case 1), showing a mass in the region of the hilum of the right lung, and another along the left border of the heart. See Fig. 2 for autopsy correlation.

On the day of admission, a roentgenogram of the chest revealed "considerable widening of the upper mediastinum and a small nodule at the auriculo-ventricular junction on the left. Lungs were clear." This roentgenogram was the same as the one taken in May, which is shown

in Fig. 1. The electrocardiogram was entirely normal except for minimal depression of the S-T segment in Lead IV. The urine contained a few leucocytes and many granular casts. The hemoglobin was 14.5 Gm. The leucocyte count was 17,500, with 96 per cent polymorphonuclears, 4 lymphocytes, and no monocytes or eosinophiles. The blood urea nitrogen was 19 mg. per cent. The spinal fluid on admission contained 300 erythrocytes and 34 mg. per cent of protein. Just before death it was opalescent and faintly reddish, and contained 30,000 erythrocytes and 53 mg. per cent of protein. Despite therapy the patient lapsed further into coma and died on December 18, two days after admission.

Autopsy.—Autopsy revealed numerous petechiae over the thorax, buccal mucosa, and conjunctivae. The heart was grossly somewhat enlarged. The right auricle and ventricle were normal. Four cysts were present on the left side of the heart (Fig. 2). On the posterior surface there was an intact cyst 3.5 cm. long and 1.5 cm. in the anteroposterior diameter overlying the interventricular septum and left ventricle. Between the ascending aorta and superior vena cava there was a tense ovoid

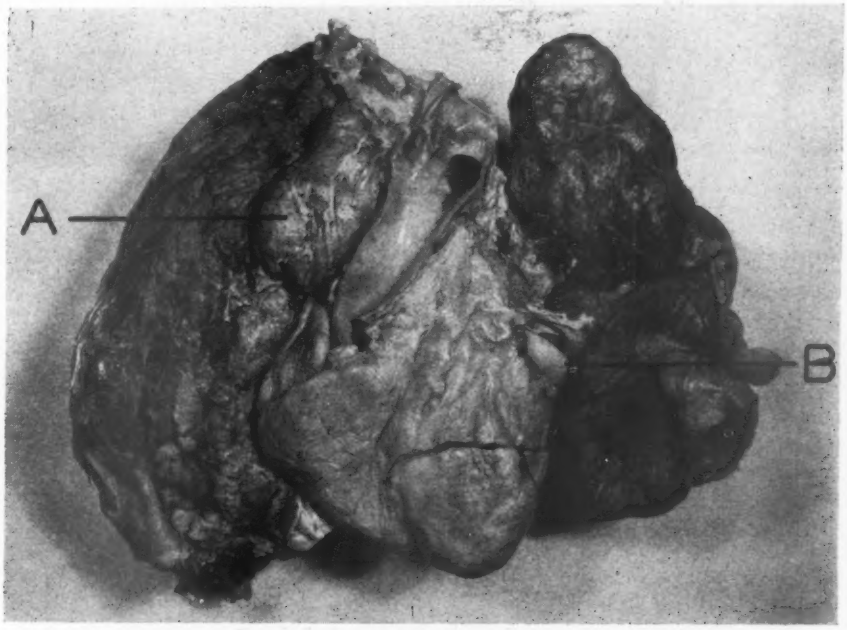


Fig. 2.—Heart and lungs of patient M. D. (Case 1), showing the paracardiac cyst at *A* and the cardiac cyst at *B*.

cystic mass 4 cm. long, 3.5 cm. in transverse diameter, and 3 cm. in the anteroposterior diameter (cyst *A* in Fig. 2). It was located outside the heart, but had destroyed by pressure all but a 4 mm. thickness of myocardium between the cyst and the cardiac lumen. No erosion had occurred into the aorta or vena cava. The third cyst was 2.4 cm. in diameter and was located on the left margin of the heart at the auriculoventricular junction. It protruded from the epicardial surface and was covered with densely adherent pericardium (cyst *B* in Fig. 2). The fourth cyst was roughly spherical, measuring 3.5 cm. in diameter, and was located on the posterolateral aspect of the left atrium (Fig. 3). It

was partly filled with blood clot and partly with gelatinous and membranous material. Its fibrous capsule had replaced the atrial myocardium. Just above the auriculoventricular junction, next to the aortic valve, there was a 1.5 cm. point of rupture.

The entire right hemisphere of the brain was somewhat atrophic, and the right temporal and occipital lobes showed areas of degeneration, but no cysts were found. Several small translucent cysts were present in the spleen.

Fig. 3.—Heart of patient M. D. (Case 1), showing the echinococcus cyst, full of blood clot, lying in the wall of the left atrium. The marker indicates the point of its rupture into the atrial cavity.

An old small echinococcus cyst was present in one kidney, and one of minute size was seen microscopically in the thyroid. No cysts were found in the lungs, liver, alimentary tract, pancreas, gall bladder, or pelvic organs.

Emboli and thrombi consisting of membranes and cyst contents were present in the left ventricle, both internal carotid arteries at their junction with the circle of Willis, the left middle cerebral artery, the celiac axis, the superior mesenteric artery, the right renal artery, and the splenic artery.

Comment.—This is an excellent illustration of involvement of the left side of the heart, with widespread embolic dissemination. The clinical picture of anaphylactic shock with embolic manifestations is classical for this condition.

Cases 2, 3, and 4 were collected from the Hydatid Registry of the Royal Australasian College of Surgeons by Dr. Louis E. Barnett, of New Zealand, who has kindly allowed us to publish their abstracts. Although data concerning these cases are few, they are being included as illustrations.

CASE 2.—"Australian: Operated on for ruptured liver cyst in August, 1933, and said to have multiple metastatic cysts elsewhere due to a leaking primary liver cyst. Details very meagre and inconclusive."

Comment.—This was apparently one of those cases in which cardiac involvement was not significant. It is unusual in that both liver and heart were involved simultaneously.

CASE 3.—"New Zealand: Little girl age 5; unsuccessful operation on December 7, 1938, for cerebral cyst. Postmortem examination revealed cyst in the left ventricle of the heart and also 2 cysts in the liver."

Comment.—This is another case in which liver and heart were simultaneously involved, and in which the cardiac cyst was discovered incidentally at autopsy.

CASE 4.—"New Zealand: Lad age 18 who died suddenly from the effects of rupture of a degenerated cyst into the left ventricle. Autopsy revealed embolic plugging of the aorta from the level of the first lumbar vertebra to the common iliac artery with hydatid material."

Comment.—This case illustrates sudden death from rupture of a cyst and massive embolic manifestations.

CASE 5.—Dr. Harold R. Dew, Professor of Surgery, University of Sydney, Australia, recently wrote us as follows concerning a case of hydatid cyst. "I saw a boy the other day with an undoubted cardiac cyst, although there is no sign of it clinically or radiographically, but he had an embolism of hydatid membrane in the femoral artery following a typical anaphylactic attack. The hydatid membrane was removed from the lumen of his artery, but his leg became gangrenous and he had to have an amputation. He will, of course, be followed up later."

Comment.—This is an illustration of one of the not uncommon ways in which a cardiac cyst makes itself known, as Dr. Dew has pointed out. It is important to recognize the possibility, however, that rupture of a pulmonary cyst into a pulmonary vein may give the same picture, as is illustrated by the following case.

CASE 6.—A young farmer, E. T., aged 22 years, was admitted to the hospital on Jan. 30, 1940, on the service of Dr. Harold R. Dew, with a story of attacks of unexplained pleurisy over the preceding two years, with some discomfort in the left side of the chest and occasional attacks of palpitation on exertion. He had had a roentgenogram in the country, and the diagnosis of cardiac hydatid cyst had been made.

On examination he appeared to be a very healthy and well-developed young man. The pulse rate was 74, the blood pressure, 124/88, and the temperature, normal. His chest showed a slight increase in size on the left; the apex beat was in the fifth intercostal space, 4½ inches from the midline. An area of dullness continuous with the cardiac dullness extended out to the scapular line and up as far as the third rib. The vocal resonance and vocal fremitus were diminished over this area, but were present below towards the left base posteriorly. The heart sounds were normal, and an electrocardiogram, taken later, showed no abnormality.

Fig. 4.—Roentgenogram of the chest in Case 6, showing the rounded tumor mass which at operation was found to be a parapericardial hydatid cyst of the left lung. The small lead shot was used as a marker.

Nothing abnormal was detected in the other organs. Roentgenograms revealed an oval shadow which was continuous with the cardiac shadow above and to the left (Fig. 4). The diagnosis of hydatid cyst in close contact with the heart was made. The Casoni intradermal test was positive.

Operation, on Feb. 8, 1940, was performed under gas and oxygen anesthesia. Thoracotomy, with removal of 3 inches of the seventh rib

in the midaxillary line, was undertaken. The pleura was found adherent (suspected because of the previous pleuritic attacks), the cyst was evacuated (about 2½ pints of fluid were obtained), the laminated membrane was removed, the cavity was swabbed out, and a drainage tube was inserted; the skin incision was loosely closed. During the operation the wall of the left ventricle was felt through the pericardium, which made up part of the adventitia of the cyst.

During the first few days after operation the patient had some interesting attacks of tachycardia and cardiac distress which I believe were due to sudden dislocation of the heart towards the large cavity to the left. These subsided after a few days. He had a mild, passive, pleural effusion which cleared up without any treatment in about ten days. He was discharged March 10, 1940. Roentgenograms now showed that the left hemithorax was normal.

Comment.—This patient had a parapericardial cyst of the left lung; the case is included as an illustration of the diagnostic difficulties encountered in differentitating cardiac from extracardiac cysts.

Cases 7 and 8 are from the files of the Peter Bent Brigham Hospital. Although both have been reported previously,[51, 78, 79] Case 7 was not suspected at the time as being one of cardiac cyst, and Case 8 seems appropriate for emphasizing the typical features of rupture of a cardiac cyst. In these reports there was no mention of cardiac cysts.

CASE 7 (S28014).—M. G., a 41-year-old Italian photographer, was referred to the Peter Bent Brigham Hospital on Jan. 18, 1927, with a diagnosis of brain tumor. His illness began with the insidious onset of headache over a period of two years, followed by failure of vision in the right eye and slight loss of memory.

Physical examination revealed weakness on the left side, left homonymous hemianopsia, and bilateral choked disks of 2½ diopters. Neurologic examination was otherwise negative. The heart sounds were regular and of good quality.

A stereoscopic roentgenogram of the chest revealed a small area of infiltration at the apex on the left, largely fibrosed and partly calcified. The lungs elsewhere were normal. The mediastinal and cardiac contours were not remarkable. Ventriculograms revealed dilatation of both lateral ventricles and displacement of the third ventricle to the left, suggesting a tumor of the right occipital lobe. Operation was delayed for several days, and the patient suddenly became restless and vomited on several occasions. He had an attack of unconsciousness lasting about one minute. The following day he had a severe headache and was restless. A few hours later he became drowsy, and by afternoon was unconscious; he was ashen, and his respiratory rate was 8 per minute, with long periods of apnea. He was immediately given 75 c.c. of 15 per cent sodium chloride solution intravenously, and improved. A right subtemporal decompression was performed that evening, and ten days later hydatid cysts were removed from the right occipital lobe. After a somewhat stormy convalescence, recovery was excellent for a period of several years. In 1931, however, he began to have epileptic attacks, usually after a bout of drinking. In 1938 he had to be institutionalized because of the development of paranoid tendencies. When last examined by Dr. Louise Eisenhardt, in July, 1942, he had a mild left-sided hemi-

paresis, with left homonymous hemianopsia. In addition, he had a convulsive state which started on the left side and later became generalized. Mentally he showed retention defects, with defective recent memory. His main difficulty was his paranoid state. No direct evidence of cardiac or pulmonary involvement with cysts has yet been obtained.

Comment.—Multiple echinococcus cysts of the occipital lobe were found in this patient at operation. He has since developed paranoid tendencies. Dumont[40] and Dew[43] feel that such cases are almost certainly secondary to cardiac involvement, but ultimate decision must await the development of changes in the roentgenograms or post-mortem examination to ascertain whether the source was lungs or heart.

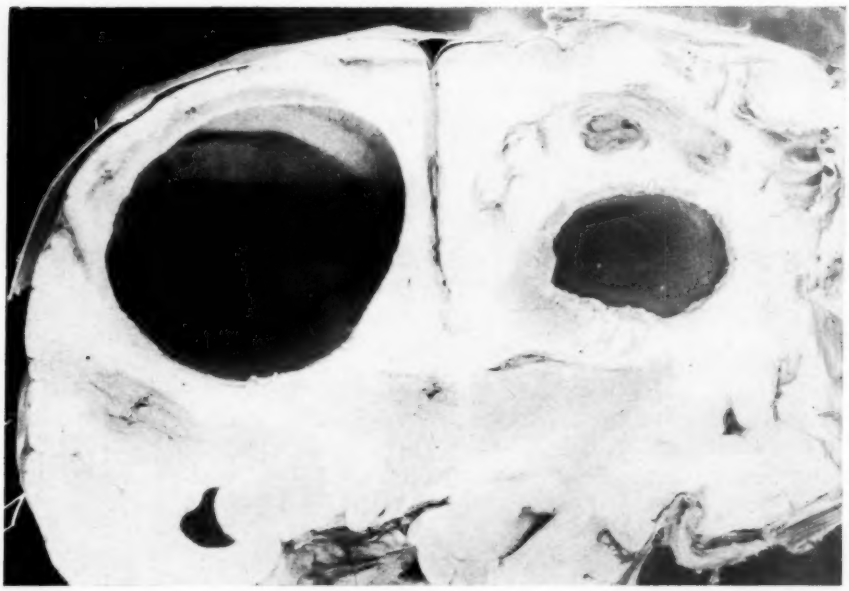


Fig. 5.—Cross section of brain of patient L. C. (Case 8), showing the two large cerebral echinococcus cysts.

CASE 8 (S636).—L. C., a 24-year-old, Italian-born laborer, was admitted to the Peter Bent Brigham Hospital Nov. 29, 1913, with a history of diffuse headache and gradual loss of use of the right arm for two months, and numbness and weakness of the right leg for one month. These symptoms had gradually increased in severity, making walking difficult. For one week before admission, he had a speech defect. The family history and past history were noncontributory except that the patient had had malaria one year previously.

On physical examination the patient had right homonymous hemianopsia. The optic discs were slightly choked. The right pupil was larger than the left. Partial motor aphasia was present. The heart was entirely normal in size and shape; the sounds were normal, of good quality, and without murmurs. There were slight dullness and bronchovesicular breathing at both apices, more pronounced on the right than on the left. The liver was not enlarged. The edge of the spleen was just palpable. The left arm was normal. The right arm was paralyzed with-

out atrophy. Although the legs were normal with respect to strength and sensation, some ataxia was noted bilaterally with the heel to knee test. The arm reflexes on the left were not obtained; those on the right were hyperactive. The knee jerks were bilaterally hyperactive. The Babinski, Oppenheim, and Gordon tests were negative; the Romberg test was positive.

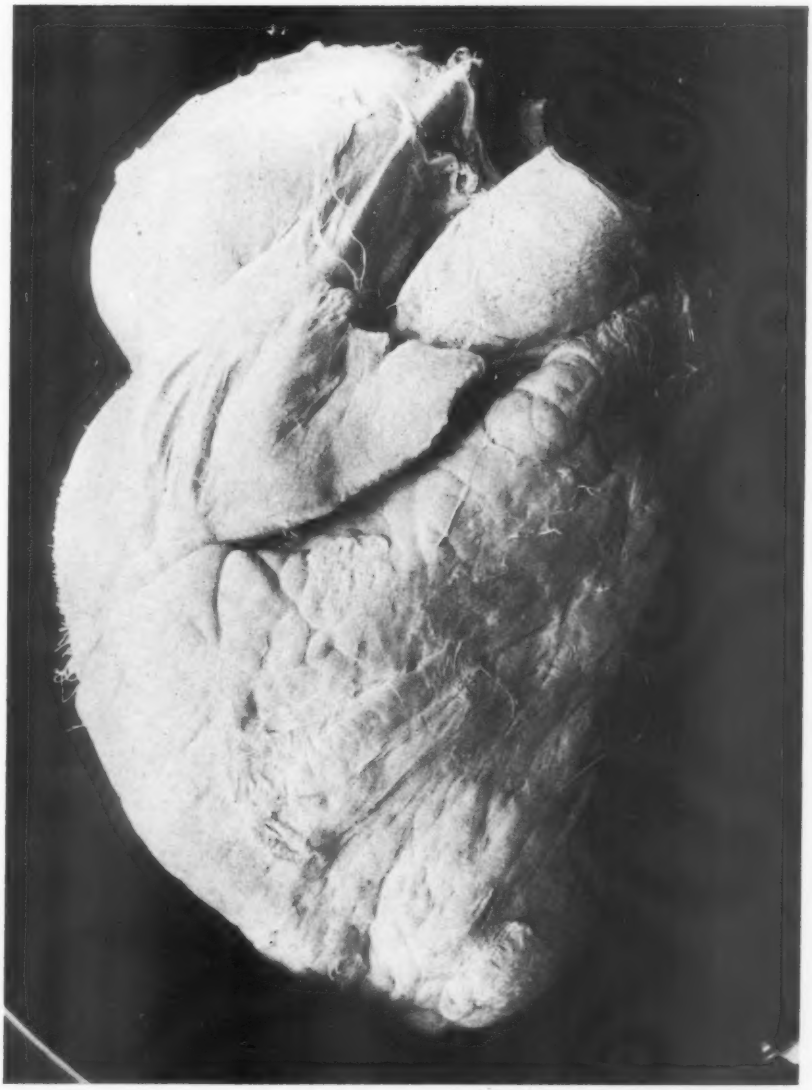


Fig. 6.—Heart of patient L. C. (Case 8), showing large mass attached to the superior portion of the right auricle.

A roentgenogram of the skull showed nothing abnormal. The blood Wassermann reaction was negative. Urine analysis was negative. The leucocyte count was 7,500, with 74 per cent neutrophiles and 7 per cent eosinophiles. The spinal fluid was under normal pressure; there were

9 cells per cubic millimeter; tests for globulin and the Wassermann reaction were negative. An echinococcus complement fixation test on the patient's serum postoperatively was reported as positive.

The patient shortly became drowsy, restless, and finally stuporous, and developed complete motor aphasia. On Dec. 4, 1913, Dr. Cushing removed three echinococcus cysts, the size of golf balls, from the left temporal region.

After the operation the patient was temporarily improved, but soon developed signs of an increase in intracranial pressure. The bone flap was eventually removed, and many aspirations of bloody yellow fluid were performed subsequently. Re-exploration was done March 3, 1914,

Fig. 7.—Heart of patient L. C. (Case 8), showing the cystic mass (ruptured post mortem) lying in the cavity of the left auricle.

but no other cyst was found. After each aspiration the patient was better, and at times was able to walk and use his right arm to some extent. As signs of an increase in intracranial pressure returned he would become worse. Five and one-half months after admission to the hospital, in May, he began to grow worse rapidly, with loss of appetite and emaciation. In June he became stuporous, and died on June 14.

Autopsy revealed echinococcus cysts in the brain and heart, but not in the liver, lungs, or any other organ. In the brain there was a cyst

8 cm. in diameter in the right occipital region, and another 3½ cm. in diameter in the left midhemisphere, extending posteriorly to the occipital lobe (Fig. 5). The heart weighed 410 grams with its cyst attached. Attached to the superior portion of the right auricle and running posteriorly to the level of the inferior region of the heart, was a large mass covering the base of the heart (Fig. 6). The mass was fluctuant and was approximately 8 cm. in diameter. It was slightly lobulated. It had no connection with the vessels or the chambers of the heart, but was closely connected to the walls of the auricle. In the left auricle a mass about 3 cm. in diameter was found to be adherent to the auricular septum, hanging from its superior pole down into the auricle, making a mass possibly one-third as large as the capacity of the chamber itself. The wall of this cyst chamber was about 1 mm. in thickness; it was white and rather friable. In removing the heart it was apparently ruptured (Fig. 7). Hooklets were demonstrable in the cyst contents from both brain and cardiac cysts. No scolices were seen.

Comment.—This is another case which illustrates cerebral cysts secondary to primary cysts of the heart; the existence of the cardiac cyst was unsuspected at the time of the brain operation. The cyst in the left auricle was of the pedicle type, but had given rise to no cardiac signs or symptoms.

The authors wish to acknowledge their sincere gratitude to Professor H. R. Dew, of Sydney, Australia, and Sir Louis Barnett, of New Zealand, for the use of cases and advice; to Drs. José Arce, Pedro Cossio, and José M. Jorge, of Argentina, for advice and materials; and to Dr. A. W. Miller, of the Department of Agriculture, for statistics on echinococcosis in the United States.

REFERENCES

1. Barnett, L. E.: Gaps in Our Knowledge of Hydatid Disease: Plea for Further Research and Tribute to Professor Félix Dévé of Rouen, Australian & New Zealand J. Surg. **4**: 211, 1935.
2. Arce, J.: Hydatid Disease (Hydatidosis). Pathology and Treatment, Arch. Surg. **42**: 1, 1941.
3. Attwood, C. J., Sargent, W. H., and Taylor, F.: Echinococcus Cyst of the Heart; Report of a Case, Ann. Int. Med. **15**: 1109, 1941.
4. Dévé, F.: Les kystes hydatiques primitifs multiples chez l'homme, Compt. rend. Soc. de biol. **80**: 859, 1917.
5. Thomas, J. D.: Hydatid Disease With Special Reference to Its Prevalence in Australia, Sydney and London, 1894.
6. Bobowicz, A.: Des hydatides du coeur chez l'homme et en particulier des hydatides flottnates, Thesis #287, Paria, 1887.
7. Cerné, A.: Kystes hydatiques multiples du foie, kyste du coeur; mort subite, Normandie Méd., Rouen **20**: 1, 1905.
8. Anderson, M. C.: Two Cases of Embolism—One the Result of Aortic Valve Disease, the Other of Hydatid Disease of the Heart, Glasgow M. J. **4**: 316, 1871-1872.
9. Charcot, J. M., and Davaine, C.: Hydatides du cerveau et du coeur, Compt. rend. Soc. de biol. **47**: 273, 1861.
10. Coote, H.: Hydatid Cyst Imbedded in the Anterior Wall of the Left Ventricle of the Heart, Med. Times & Gaz. London **8**: 156, 1854.
11. Evans: Case report, Australian Med. Gaz. **1**: 169, 1882.
12. Graham, J.: Hydatid Disease in Its Clinical Aspects, Edinburgh and London, 1891.
13. Köhler, R.: Grosses Axillar-Aneurysma durch einen Echinokokkus der Gefässscheide verursacht, Berl. klin. Wchnschr. **26**: 1077, 1889.
14. Moxon, W.: Hydatid of the Heart, Obliterating by Its Pressure the Coronary Sinus, Tr. Roy. Path. Soc. Lond. **21**: 99, 1870.
15. Renault: Kyste hydatique du coeur. Kystes hydatiques de la rate, Bull. Soc. Anat. Paris **7**: 124, 1882.

16. Ward, N.: Acephalocysts in the Substance of the Heart, Tr. Roy. Path. Soc. Lond. **1**: 225, 1847-1848.
17. Welling, Louis de: Des kystes hydatiques du coeur. Thesis, Paris, 1872.
18. Williams, W. H.: Hydatiden in dem Herzen eines Kindes, Schmidt's Jahrb. **9**: 29, 1836.
19. Dévé, F.: De l'échinococcose secondaire. Thesis #628, Paris, 1901.
20. Altmann, C. A.: Hydatid of Heart—Rupture Into Left Auricle and Plugging of Left Carotid Artery, Intercol. Med. J. Australia **7**: 573, 1902.
21. Oesterlen, O.: Ueber Echinococcus im Herzen, Virchows Arch. f. path. Anat. **42**: 404, 1868.
22. Dévé, F.: De l'échinococcose secondaire embolique, Compt. rend. Soc. de biol. **53**: 608, 1901.
23. Dévé, F.: Échinococcose cérébrale métastatique, Compt. rend. Soc. de biol. **81**: 633, 1918.
24. Dévé, F.: La rupture iterative des kystes hydatiques du coeur, Compt. rend. Soc. de biol. **79**: 514, 1916.
25. Dévé, F.: L'échinococcose chez l'enfant. Intérêt doctrinal de son étude, Compt. rend. Soc. de biol. **79**: 911, 1916.
26. Dévé, F.: Sur l'échinococcose secondaire du péricard, Compt. rend. Soc. de biol. **78**: 734, 1915.
27. Dévé, F.: Sur l'origine des vesicules hydatiques filles, Compt. rend. Soc. de biol. **54**: 529, 1902.
28. Dévé, F., and Boppe, M.: L'échinococcose pulmonaire métastatique, dans ses relations avec l'age des malades et le siège du kyste primitif, Compt. rend. Soc. de biol. **79**: 913, 1916.
29. Marten, R. H., and de Crespigny, C. T. C.: Notes on a Case of Hydatid of the Heart, M. J. Australia **8**: 287, 1921.
30. Long, W. J.: Hydatid Disease in the Left Ventricular Wall of the Heart, M. J. Australia **19**: 701, 1932.
31. Grulee, C. G.: Echinococcus Disease of the Heart, With a Report of a Case, Surg., Gynec. & Obst. **1**: 328, 1905.
32. Lyon, I. P.: A Review of Echinococcus Disease in North America, Am. J. M. Sc. **123**: 124, 1902.
33. Magath, T. B.: Hydatid Disease (Echinococcus) in North America, Pennsylvania M. J. **44**: 813, 1941.
34. Miller, A. W.: Personal communication.
35. Salmon, D. E.: Pathological Conditions Found in Meat Inspection, J. A. M. A. **36**: 867, 1901.
36. Ward, H. B.: Hydatid Disease, Wood's Reference and Handbook of the Medical Sciences **2**: 788, 1901.
37. Riley, W. A.: Maintenance of Echinococcus in the United States, J. Am. Vet. M. A. **95**: 170, 1939.
38. Ofeigsson, O. J.: Hydatid Disease in Iceland, Proc. Staff Meet., Mayo Clin. **12**: 240, 1937.
39. Barnett, L. E.: The Incidence of Hydatid Disease in New Zealand, New Zealand M. J. **40**: 273, 1941.
40. Dumont, M.: L'échinococcose cérébrale métastatique. Thesis, Toulouse, July, 1918.
41. Dew, H. R.: Some Aspects of Echinococcus Disease, Surgery **2**: 363, 1937.
42. Magath, T. B.: Echinococcus Disease: Etiology and Laboratory Aids to Diagnosis, M. Clin. North America **5**: 549, 1921.
43. Dew, H. R.: Hydatid Disease of the Brain, Surg., Gynec. & Obst. **59**: 321, 1934.
44. Dévé, F., and Dumont, M.: L'échinococcose cérébrale, dans ses rapports avec l'age des malades, Compt. rend. Soc. de biol. **79**: 1000, 1916.
45. Dew, H. R., Kellaway, C. H., and Williams, F. E.: The Intradermal Reaction in Hydatid Disease and Its Clinical Value, M. J. Australia **12**: 471, 1925.
46. Fairley, N. H.: Researches on the Complement Fixation Reaction in Hydatid Disease, Quart. J. Med. **15**: 244, 1922.
47. Fleig, C., and Lisbonne, M.: Quelques données pratiques sur le précipitodiagnostic de l'échinococcose, Presse méd. **17**: 832, 1909.
48. Ghedini, G.: Richerche sul siero di sangue di individuo affetto da cisti da echinococco e sul liquido in essa contenuto, Gazz. de osp. **27**: 1616, 1906.
49. Senekji, H. A.: Polysaccharide Scolex Antigen for the Immunological Diagnosis of Hydatid Disease, Tr. Roy. Soc. Trop. Med. & Hyg. **34**: 401, 1941.
50. Welsh, D. A., Chapman, H. G., and Storey, J. C.: Some Applications of the Precipitin Reaction in the Diagnosis of Hydatid Disease, Lancet **1**: 1103, 1909.

51. Cairns, H.: A Study of Intracranial Surgery, Med. Res. Counc. Spec. Rep. Ser. #125, London, 1929.
52. Foresti, C. B., and Bonaba, J.: Un cas de kystes hydatiques viscéraux multiples (coeur, cerveau, reins). Rupture de l'un des kystes du coeur dans l'oreillette gauche. Constatation à l'autopsie de vésicules-filles libres à l'intérieur des cavités cardiaques gauches. Intégrité du foie et des poumons, Bull. et mém. Soc. méd. d. hôp. de Paris **38**: 262, 1914.
53. Giles, W. A.: Pyaemia Following Upon Chronic Suppurative Inflammation of the Middle Ear, and Associated With Hydatid Cysts of the Brain, Heart and Kidney, Intercol. Quart. J. Med. & Surg. **1**: 355, 1894-1895.
54. Mettenheimer, C.: Ein Fall von Echinococcus des Herzens, Memorabilien Heilbr. **22**: 337, 1877.
55. Barnett, L. E.: Personal communication.
56. Berg, T.: Bericht über die Krankenpfleger junger Kinder in meiner Abtheilung des allgemeinen Waisenhauses zu Stockholm in Jahre 1842, J. f. Kinderkr. **3**: 328, 1843.
57. Guglielmi: Deux kystes à échinocoques trouvés dans le ventricle gauche d'une indigène, J. Med. & Pharm. Algérie **1**: 92, 1877.
58. Landouzy: Kyste hydatique du péricarde viscérale, Bull. Soc. Anat. Paris **45**: 309, 1870.
59. Martin-Durr: Kyste hydatique de la paroi antérieure du ventricle gauche, Bull. Soc. Anat. Paris **64**: 131, 1889.
60. Mayet: Kystes hydatiques multiples (foie et coeur), Bull. Soc. Anat. Paris **70**: 50, 1895.
61. Olmer: Présentation anatomique: Kyste hydatique du coeur chez un vieillard artériosclereux, mort de pneumonie, Marseille-méd. **36**: 218, 1899.
62. Pelissier, A.: Kyste hydatique du coeur, Bull. Med. Soc. Anat. Paris **87**: 257, 1912.
63. Rokitansky: Schmidt Jahrb. **116**: 194, 1862.
64. Thorel, C.: Pathologie der Kreislauforgane des Menschen, Ergebn. d. allg. Path. u. path. Anat. **17**: 687, 1915.
65. Verco, J. C., and Poulton, B.: Hydatid of Brain, Australasian Med. Gaz. **27**: 290, 1908.
66. Christopherson, J. B.: A Case of Hydatid Cyst of the Left Ventricle, Together With Some Remarks on Hydatid Disease in the Anglo-Egyptian Sudan, J. Trop. Med. **12**: 317, 1909.
67. Goodhart, J. F.: Cured Hydatid Cyst in the Wall of the Heart, Trans. Roy. Path. Soc. London **27**: 72, 1876.
68. Hatieganu, I., Vasiliu, T., and Moga, A.: Le kyste hydatique du coeur simulant un anéyrisme, Arch. d. mal. du cœur **29**: 72, 1936.
69. Heimann, H. L.: Hydatid Cyst in the Heart, Brit. M. J. **1**: 801, 1928.
70. Knaggs, W. H. E.: Hydatids of the Heart, Lancet **1**: 29, 1896.
71. Peacock, T. B.: Hydatid Cyst Embedded in the Walls of the Heart, Trans. Roy. Path. Soc. London **24**: 37, 1873.
72. Vielle, G.: Apropos d'un kyste hydatique du coeur, Soc. de méd. mil. franc., Bull. mens. **25**: 116, 1931.
73. Wilks: Loose Hydatid in the Heart, Trans. Roy. Path. Soc. London **11**: 71, 1859-1860.
74. Wood, A. J.: Hydatid of Heart, Intercol. Med. J. Aust. **6**: 136, 1901.
75. Bosch, R. G., and Mosto, D.: Hydatidosis cardíaca, Prensa med. argent. **24**: 308, 1937.
76. Domantke, G.: Kyste hydatique du coeur, Bull. Soc. Anat. Paris **70**: 122, 1895.
77. Rendu: Hydatides du cerveau du coeur et des reins. Arrêt de developpement de l'utérus et des ovaires, Bull. Soc. Anat. Paris **53**: 581, 1878.
78. Horrax, G., and Putnam, T. J.: Distortions of the Visual Fields in Cases of Brain Tumor. VII. The Field Defects and Hallucinations Produced by Tumors of the Occipital Lobe, Brain **55**: 499, 1932.
79. Walker, C. B.: Further Observations on the Hemiopic Pupillary Reaction Obtained With a New Clinical Instrument, Tr. Sect. Ophth., A. M. A., 318, June, 1914.
80. Dew, H. R.: Personal communication.

HEART DISEASE IN THE SOUTH

I. A Statistical Study of 1,045 Cardiac Deaths

Alice Baker Holoubek, M.D.
New Orleans, La.

SEVERAL interesting studies of the incidence and etiological types of heart disease, based on clinical material from every section of the United States, have been published.[1-14, 19] Relatively few of these surveys[3, 5, 6, 9, 15] originated in the South, and fewer[19] considered autopsy material. One general impression gained from these reviews was that rheumatic heart disease is relatively insignificant in the South. The surprising number of patients with rheumatic heart lesions encountered on the wards and in the clinics of the Charity Hospital of Louisiana at New Orleans instigated this study. This was later expanded to a statistical study of cardiac deaths at this institution. The autopsy records of the years 1935 to 1940, inclusive, were reviewed, and all deaths due primarily to heart disease were studied* and classified etiologically according to the criteria of Classification of Heart Disease of the American Heart Association. The diagnoses were made on autopsy data, and, in cases of heart disease which does not cause characteristic anatomic abnormalities, on clinical observations. In those cases in which two or more etiological types of heart disease were present, the one which was the cause of death determined the classification under which it was included, and the coexisting types were listed as associated conditions. In a few cases this was impossible, and these were listed as a combined group. Since this survey was confined to charity cases, it covered heart disease in the lower economic groups only.

A total of 8,313 autopsies were performed during this period. In this series, 1,045 deaths (12.6 per cent) were attributed primarily to heart disease. The majority of these persons (665, or 63.6 per cent) were Negroes and the remainder (380, or 37.4 per cent) were white. The age at death varied from stillborn to 98 years. There were 704 males (67 per cent) and 341 females (33 per cent). Figs. 1 and 2 show the causes of cardiac deaths and the incidence of each in the white and Negro races.

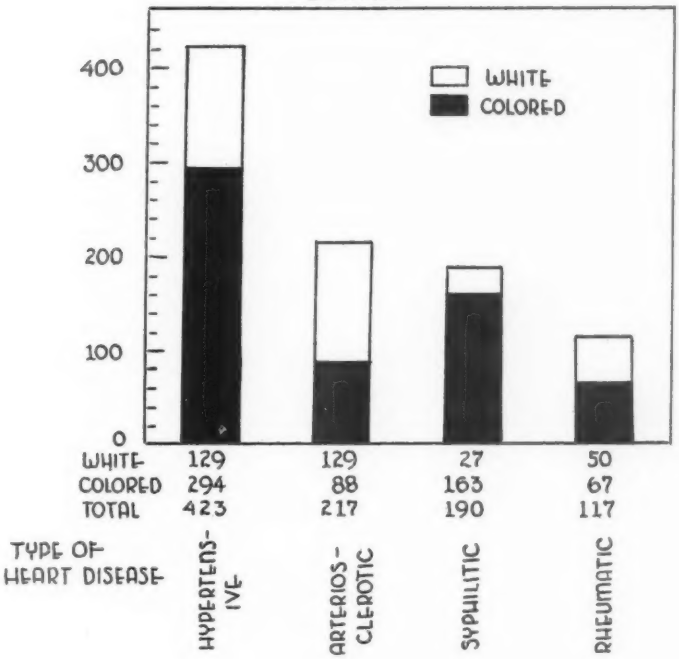
Hypertensive.—The greatest number of cardiac deaths were due to hypertensive heart disease. Four hundred twenty-three persons (40.5 per cent of the entire series) died of this condition, of whom 294

From the Department of Medicine of the Louisiana State University School of Medicine and the Charity Hospital of Louisiana at New Orleans.

Received for publication April 15, 1944.

*The members of the Pathology Department of the Hospital and of the Louisiana State University School of Medicine were very cooperative, and assisted in the study of records which proved difficult to interpret.

THE INCIDENCE OF THE MOST FREQUENT CAUSES OF CARDIAC DEATHS

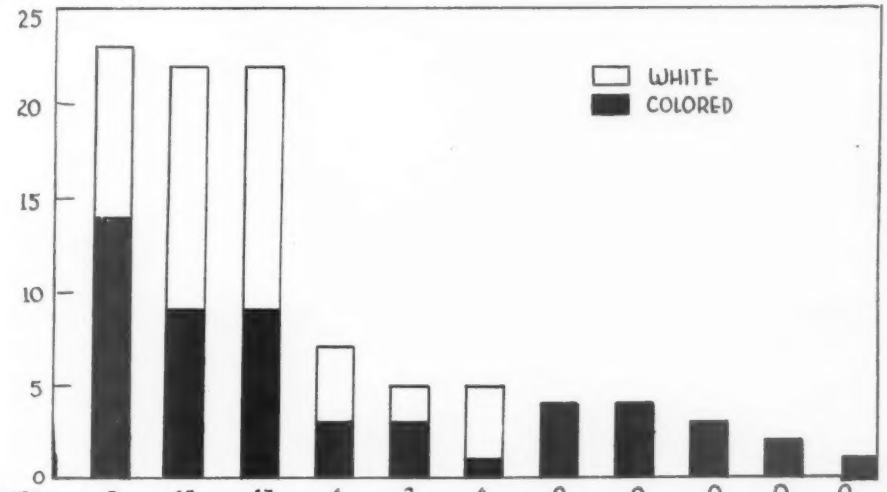


	HYPERTENSIVE	ARTERIOSCLEROTIC	SYPHILITIC	RHEUMATIC
WHITE	129	129	27	50
COLORED	294	88	163	67
TOTAL	423	217	190	117

TYPE OF HEART DISEASE

Fig. 1.

THE INCIDENCE OF THE LESS FREQUENT CAUSES OF CARDIAC DEATHS



	CONGENITAL	TOXIC	BACTERIAL	ANEMIA	AVITAMINOSIS	COMBINED	HYPERTHYROIDISM	PULMONARY DISEASES	OTHER	UNKNOWN	TRAUMA
WHITE	9	13	13	4	2	4	0	0	0	0	0
COLORED	14	9	9	3	3	1	4	4	3	2	1
TOTAL	23	22	22	7	5	5	4	4	3	2	1

TYPE OF HEART DISEASE

Fig. 2.

(69.5 per cent) were Negroes and 129 (30.5 per cent) were white. Of the Negro persons, 185 (63 per cent) were males. The percentage of males was also higher in the white race, namely, 70.6 per cent, or 101 cases. The distribution according to age is clearly shown in Fig. 3. The most commonly associated cardiac complication in this group was arteriosclerosis, which occurred in 143 cases (33.6 per cent). Rheumatic heart disease was present in 17 (4 per cent), and syphilitic heart disease in 8 (1.8 per cent).

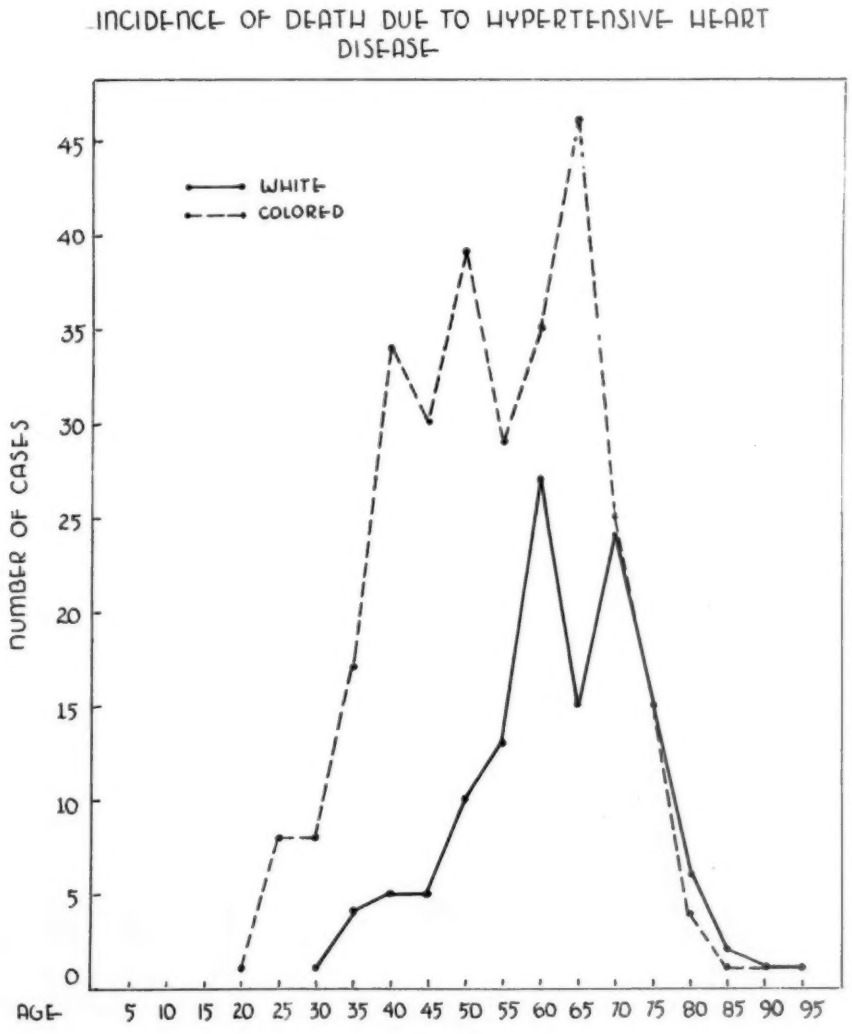


Fig. 3.

Arteriosclerotic.—Two hundred seventeen deaths (20.7 per cent) were due primarily to cardiac arteriosclerosis. The incidence in the white race was 129 (59.4 per cent), as compared to 88 (40.6 per cent)

in the Negro race (Fig. 4). This group included 117 cases (53.9 per cent) in which there was pathologic evidence of coronary occlusion, myocardial infarction, or both. The percentage of occlusion and/or infarction in the males with arteriosclerotic heart disease was 57.3 per cent (white), as compared to 49.9 per cent (Negro); in the females it was 54.5 per cent (white) and 51.5 per cent (Negro). Eleven, or 5.1 per cent, of the patients with arteriosclerotic heart disease died of dissecting aneurysm (only two of these were females).[17] Complicating cardiac conditions included hypertension, 47 cases (21.6 per cent), rheumatic heart disease, 10 cases, and syphilitic heart disease, 3 cases.

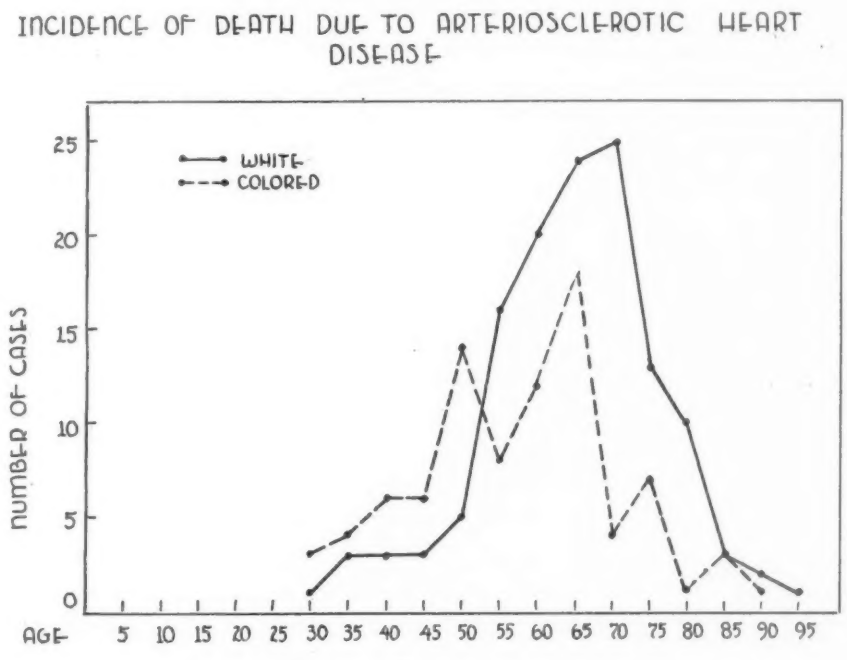


Fig. 4.

Syphilitic Cardiovascular Disease.—One hundred ninety (18.2 per cent) of the cardiac deaths were found to be due to syphilitic cardiovascular disease. The Negro race predominated, with 163 cases (86 per cent) (Fig. 5). The incidence of sex and race in this disease is of particular interest. There were 125 (66 per cent) Negro males, 38 (20 per cent) Negro females, 23 (12 per cent) white males, and 4 (2 per cent) white females. Included in this group are 77 cases in which death was due to syphilitic aortic aneurysm. It is interesting that the remaining 103 cases constitute a group in which the primary cause of death was syphilitic involvement of the heart; these comprise 10.8 per cent of the total number of cardiac deaths.

Complicating cardiac conditions in the entire syphilitic cardiovascular group included rheumatic heart lesions, 14 cases, in one of which there

were subacute bacterial vegetations on the rheumatic lesions; arteriosclerosis, 13 cases; bacterial endocarditis of the involved aortic valve, 6 cases, in 3 of which the lesions were acute, and, in the other 3, subacute; and hypertension, 5 cases.

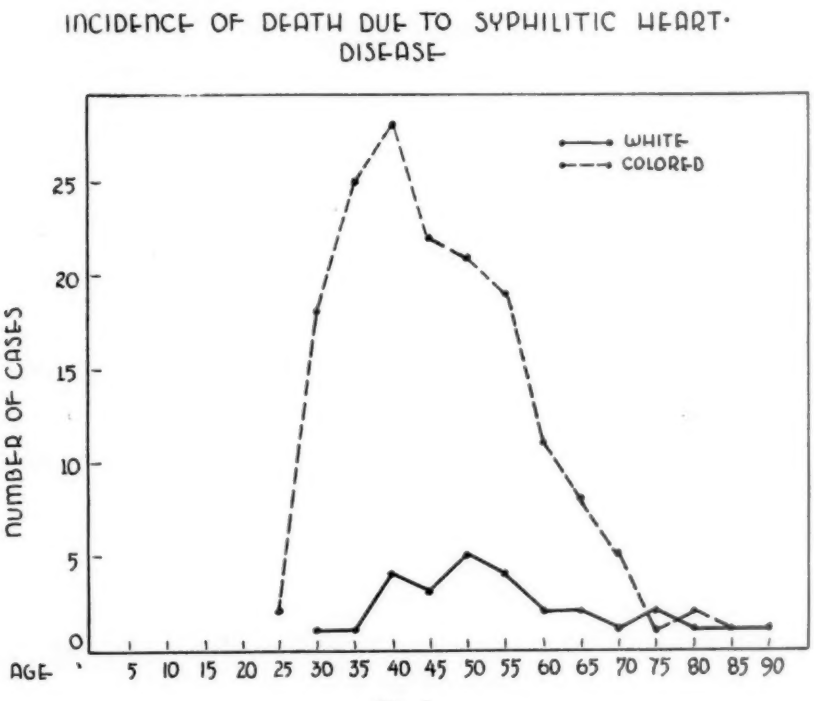


Fig. 5.

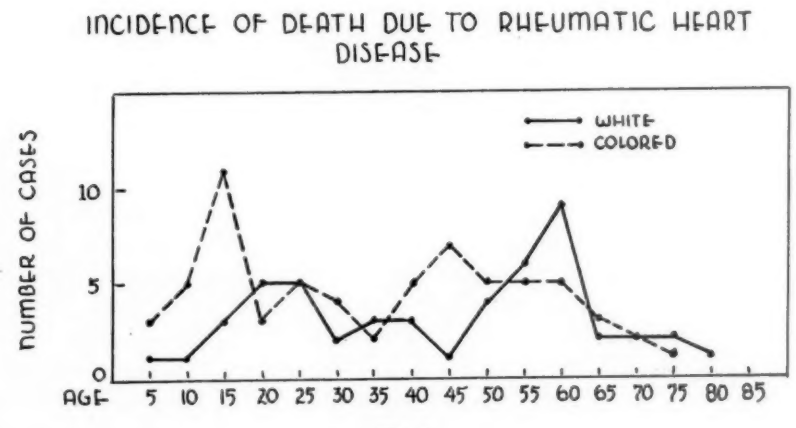


Fig. 6.

Rheumatic.—The percentage of deaths due to rheumatic heart disease was 11.1 per cent, or 117 of the entire series; 67, or 57.3 per cent, of these persons were of the Negro race. As shown in Fig. 6, there

were two age periods (10 to 15 years and 40 to 45 years) at which the highest rate of mortality occurred in the white race. There were similar peaks among the Negro patients, but these occurred 10 to 15 years later.

Complicating cardiac conditions in this group consisted of 16 cases of subacute bacterial endocarditis, 11 cases of arteriosclerosis, 5 cases of acute bacterial endocarditis, and 5 cases of hypertension.

Congenital.—Congenital cardiac lesions were the cause of 23 deaths, or 2.2 per cent of the total number of cardiac deaths. Fourteen of these persons were Negroes. The age at death varied from stillborn to 16 years. There were 15 females and 8 males. Further consideration of the varied anomalies included in this group would be too lengthy and detailed for this report. However, it is interesting that subacute bacterial endocarditis was present in only one case in this group.

Toxic.—Twenty-two deaths (2.1 per cent) were ascribed to toxic heart disease. Of these, 13 patients were white and 9 Negro (Fig. 2). The causes of the toxemia which produced these cardiac deaths were diphtheria, 12 cases; typhoid fever, 4 cases; septicemia, 2 cases; pertussis, 2 cases; bronchopneumonia, 1 case; and digitalis poisoning, 1 case.

Bacterial Infection.—Primary bacterial infection of the heart resulted in 22 (2.1 per cent) cardiac deaths. In none of these cases was there

TABLE I

SHOWING THE INCIDENCE OF EACH ETIOLOGICAL TYPE OF HEART DISEASE AS THE PRIMARY CAUSE OF DEATH, AND ALSO THE FREQUENCY WITH WHICH IT WAS PRESENT AS AN ASSOCIATED ABNORMALITY

	PRIMARY CAUSE OF DEATH		ASSOCIATED ABNORMALITIES PRESENT WHEN DEATH WAS DUE TO FOLLOWING TYPES OF HEART DISEASE						TOTAL IN THIS SURVEY	
ETIOLOGICAL TYPE OF HEART DISEASE	NUMBER	PERCENTAGE	HYPERTENSIVE	ARTERIOSCLEROTIC	SYPHILITIC	RHEUMATIC	COMBINED	TRAUMA	NUMBER	PERCENTAGE
Hypertensive	423	40.5	–	47	5	5	1	–	481	46.0
Arteriosclerotic	217	20.7	143	–	13	11	3	1	287	27.6
Syphilitic	190	18.2	8	3	–	–	2	–	203	19.4
Rheumatic	117	11.1	17	10	14	–	4	1	163	15.6
Congenital	23	2.2	–	–	–	–	2	–	25	2.4
Toxic	22	2.1	–	–	–	–	–	–	22	2.1
Bacterial infection	22	2.1	–	–	6	21	2	–	51	4.9
Anemia	7	0.7	–	–	–	–	–	–	7	0.7
Avitaminosis	5	0.5	–	–	–	–	–	–	5	0.5
Combined	5	0.5	–	–	–	–	–	–	5	0.5
Hyperthyroidism	4	0.4	–	–	–	–	–	–	4	0.4
Pulmonary disease	4	0.4	–	–	–	–	–	–	4	0.4
Other types	3	0.3	–	–	–	–	–	–	3	0.3
Unknown	2	0.2	–	–	–	–	–	–	2	0.2
Trauma	1	0.1	–	–	–	–	–	–	1	0.1

TABLE

INCIDENCE OF THE FOUR MOST IMPORTANT ETIOLOGICAL

AUTHOR	Holoubek			Laws[9]		Schwab and Schulze[5]	Stone and Vanzant[3]	Musser[15]	Maher et al.[18]
LOCALITY	New Orleans			Tennessee		Galveston	Galveston	New Orleans	Chicago
	W	N		W	N				
	%	%	%	%	%	%	%	%	%
HYPERTENSIVE	12.4	28.1	40.5	65.1	71.8	57.2	47.7	58.5	26.2
ARTERIOSCLEROTIC	12.3	8.4	20.7			20.2	13.7		24.1
SYPHILITIC	2.6	15.6	18.2	2.2	15.4	12.7	19.3	16.5	9.7
RHEUMATIC	4.7	6.4	11.1	15.3	4.3	3.4	7.3	17.6	29.2

evidence of pre-existing heart disease of any type. There were 14 cases of subacute bacterial endocarditis, 8 white patients and 6 Negro; 6 cases of acute bacterial endocarditis, 4 white patients and 2 Negro; one case (a white female) of acute suppurative myocarditis and pericarditis of postpneumonic origin; and one (a Negro female) of tuberculous pericarditis causing cardiac tamponade.

Anemia.—Seven deaths (0.7 per cent), 3 Negro patients and 4 white, were classified as due to anemia. Sickle cell anemia was the causative factor in the case of 3 Negro patients. Two were due to pernicious anemia, one to sprue, and one to chronic pulmonary hemorrhage.

Avitaminosis.—Five deaths (0.5 per cent) were classified as due to beriberi. Three of these patients were Negroes, and 2 were white. Three were females, and 2 were males. The age at death varied from 28 to 57 years.

Hyperthyroidism.—This condition caused 4 cardiac deaths (0.4 per cent). All of the patients were Negroes, and 3 of these were males. The age at death varied from 34 to 40 years.

Pulmonary Disease.—Four cardiac deaths (0.4 per cent), all among Negro patients, were attributed to primary pulmonary disease. Ayerza's disease was the cause of 3 deaths. The fourth was a case of chronic cor pulmonale secondary to pulmonary tuberculosis.

Other Types.—Under this classification we have included 3 deaths (0.3 per cent). Two were due to amyloidosis of the heart, and one was a case of acute dilatation of the heart caused by a rapidly given transfusion. All of these patients were Negroes.

Unknown.—Two Negro persons (0.2 per cent) died of heart disease of unknown origin; one had a diffuse, nonsuppurative, isolated myocarditis, and one had acute dilatation of the heart.

Trauma.—There was one death (0.1 per cent) due to a stab wound of the heart which severed the anterior descending coronary artery. This patient had a definite coincidental rheumatic lesion of the heart.

Combined.—This group consisted of 5 cases (0.5 per cent), 4 white patients and 1 Negro. A white woman, aged 78 years, had a syphilitic saccular aneurysm of the aortic arch, 6 cm. in diameter, which terminated in a dissecting aneurysm extending to the common iliac vessels.

TABLE II

TYPES OF HEART DISEASE IN DIFFERENT GEOGRAPHICAL AREAS

DePorte[8]	White and Jones[4]	Geiger et al.[11]	Chavez[16]	Viko[12]				Clawson[19]
New York	New England	San Francisco	Mexico	Virginia	New York City	New England	Rocky Mountains	Minneapolis
%	%	%	%	%	%	%	%	%
21.1	29.2	6.8	13.6	32.6		21.7	14.9	55.5
8.1	35.7	24.9	28.3	32.4	22.3	26.3	21.1	6.2
4.6	3.9	7.2	11.2	7.8	8.6	2.7	1.1	7.0
27.2	39.5	22.2	41.0	15.6	42.7	29.3	41.0	18.6

A Negro man, aged 55 years, showed evidence of rheumatic, hypertensive, and arteriosclerotic heart disease, with fenestration of the cusps of the aortic and pulmonary valves and an aneurysm of the right coronary artery 2.5 cm. in diameter. A white man, aged 76 years, was found to have rheumatic and syphilitic valvular lesions and coronary arteriosclerosis. Two white women, 23 and 30 years of age, had congenital and rheumatic heart disease complicated by subacute bacterial endocarditis.

Table I shows the frequency with which each etiological type of heart disease was present as an associated abnormality and as primary cause of death.

DISCUSSION

It must be remembered that the majority of previous reports are based on clinical data only, whereas this report is based on autopsy observations in cases in which death was due to heart disease. Table II compares our observations with selected representative reports from different geographical areas. Only the four most frequent etiological types of heart disease are considered.

The hypertensive group includes over twice as many Negroes as whites, and the males predominate in both races. The peak of the number of deaths according to age begins approximately 20 years earlier in the Negro race than in the white race (40 years of age as compared to 60 years), and declines at approximately the same age (75 years of age in each). The high incidence of hypertensive heart disease in this survey of autopsy cases verified the similarly high clinical incidence reported from the Southern states.[3, 5, 9, 15] Here the high percentage of Negro patients is undoubtedly an important factor.

In the group in which death was due to arteriosclerotic heart disease there were more white than Negro patients. About one-half (59.3 per cent) of this group showed evidence of myocardial infarction, coronary occlusion, or both. In this select group the proportion of males to females and white to Negro patients was practically the same. The age distribution in the entire group was also practically the same in the white as in the Negro race. Arteriosclerotic heart disease was found to occur with similar frequency in reports from practically every section

of the country, including Mexico. In this survey, hypertensive and arteriosclerotic heart disease caused death in 640 cases, or 61.2 per cent of the total number of cardiac deaths. This includes 190 cases (18.1 per cent) in which both conditions were present.

The greatest percentage of deaths due to syphilitic heart disease was in the Negro race; the ratio was roughly 6:1. There were four times as many males as females, considering both races. The incidence of this disease in this survey was about the same as in other reports originating in the South, but is much higher than that reported from Northern clinics, as would be expected.

The incidence of rheumatic heart disease was found to be higher than in 4 out of 6 reports originating in Southern states, but was much less than in the Northern states. It is interesting that Chavez[16] found an incidence of 41 per cent in Mexico City. This again would tend to disprove the common belief that rheumatic heart disease is rare in semitropical and tropical regions.

SUMMARY

Autopsy observations in 1,045 cases of death due to heart disease at the Charity Hospital of Louisiana in New Orleans over a period of six years were studied statistically. Table III gives the etiological distribution of these deaths in order of frequency:

TABLE III

ETIOLOGY	NUMBER	PERCENTAGE
Hypertensive heart disease	423	40.5
Arteriosclerotic heart disease	217	20.7
Syphilitic cardiovascular disease	190	18.2
Rheumatic heart disease	117	11.1
Congenital heart disease	23	2.2
Toxic heart disease	22	2.1
Bacterial infection	22	2.1
Anemia	7	0.7
Avitaminosis	5	0.5
Combined	5	0.5
Hyperthyroidism	4	0.4
Pulmonary disease	4	0.4
Other types	3	0.3
Unknown	2	0.2
Trauma	1	0.1

REFERENCES

1. Harrison, T. R., and Levin, S. A.: Notes on the Regional Distribution of Rheumatic Fever and Rheumatic Heart Disease in the United States, South M. J. **17**: 914, 1924.
2. Wood, J. Edwin, Jones, T. Duckett, and Kimbrough, Ray D.: The Etiology of Heart Disease, Am. J. M. Sc. **172**: 185, 1926.
3. Stone, C. T., and Vanzant, F. R.: Heart Disease as Seen in a Southern Clinic, Cl. and Path. Survey, J. A. M. A. **89**: 1473, 1926.
4. White, P. D., and Jones, T. D.: Heart Disease and Disorders in New England, AM. HEART J. **3**: 302, 1928.
5. Schwab, E. H., and Schulze, V. E.: The Incidence of Heart Disease and of the Etiological Types in a Southern Dispensary, AM. HEART J. **7**: 223, 1931.

6. Schwab, E. H., and Schulze, V. E.: Heart Disease in the American Negro of the South, AM. HEART J. 7: 710, 1932.
7. Wyckoff, J., and Lingg, C.: II. Etiology in Organic Heart Disease, AM. HEART J. 1: 446, 1926.
8. DePorte, J. V.: Heart Disease in General Medical Practice. Preliminary Report of Morbidity Survey Conducted by the New York State Department of Health, AM. HEART J. 8: 476, 1933.
9. Laws, C. L.: The Etiology of Heart Disease in White and Negro in Tennessee, AM. HEART J. 8: 608, 1933.
10. Gagen, Leslie T., and Dunn, W. LeRoy: Heart Disease in Washington, D. C., M. Ann. District of Columbia 2: 112, 1933.
11. Geiger, J. C., Sampson, J. J., Miller, R. C., and Gray, J. C.: A Survey of Heart Disease Morbidity in San Francisco, AM. HEART J. 12: 137, 1936.
12. Viko, L. E.: Heart Disease in the Rocky Mountain Region, AM. HEART J. 6: 264, 1930.
13. Maher, C. C., Sitler, W. W., and Elliot, R. A.: Heart Disease in the Chicago Area, J. A. M. A. 105: 263, 1935.
14. Dauer, C. C.: Mortality Rates of Organic Disease of the Heart by Geographical Areas in the United States, AM. HEART J. 10: 955, 1935.
15. Musser, J. H.: Some Consideration of Several Important Etiological Types of Heart Disease, New Orleans M. & S. J. 86: 356, 1933.
16. Chavez, Ignacio: The Incidence of Heart Disease in Mexico, AM. HEART J. 24: 88, 1942.
17. Holland, L. F., and Bayley, R. H.: Dissecting Aneurysm, AM. HEART J. 20: 233, 1940.
18. Decherd, George M., and Schenken, John R.: Malignant Hypertension, New Orleans M. & S. J. 90: 275, 1938.
19. Clawson, B. J.: Incidence of Types of Heart Disease Among 30,265 Autopsies With Special Reference to Age and Sex, AM. HEART J. 22: 607, 1941.

INCIDENCE OF HEART DISEASE AND RHEUMATIC FEVER IN SCHOOL CHILDREN IN THREE CLIMATICALLY DIFFERENT CALIFORNIA COMMUNITIES

MAJOR JOHN J. SAMPSON, M.C., ARMY OF THE UNITED STATES,
CAPTAIN PAUL T. HAHMAN, M.C., ARMY OF THE UNITED STATES,
WILTON L. HALVERSON, M.D., AND MARGERY C. SHEARER, M.D.

THIS survey was planned primarily to show the influence of climate on the incidence of rheumatic heart disease and rheumatic fever.* General impressions are given of the economic status of each community studied, but it was not possible to segregate the children according to economic strata. An attempt was made to show by history, physical examination, and home visits the relation to rheumatic disease of age, sex, race, family history, diet, housing, previous and current infections, nutritional state, and other physical characteristics of the children.

The reporting of congenital cardiovascular defects, functional heart murmurs, and hypertension was incidental to the above objectives. Likewise, the discovery of previously undiagnosed cases was reported through the school nurses to the private physicians or health departments for follow-up and care. It is hoped that with projected improvement of environmental conditions, especially housing, the data from these surveys may be used for comparison with future surveys in evaluating the results of such community improvements.

Many school cardiac surveys have been made in the United States and Great Britain,[1-20] and the prevalence of rheumatic disease in children has likewise been ascertained from the compulsory notification of rheumatic fever in Norway, Sweden, Denmark, Iceland, and certain cities in Germany and England.

Considerable differences have been reported in the prevalence of heart disease, ranging from 0.3 to 2.6 per cent, not only in different locales but even in the same community. This has been dependent on the following factors: (1) A difference in diagnostic criteria; (2) variation of the degree of skill and interest of the examiners; (3) irregular selection of samples from different age groups; (4) unawareness of socio-economic influences affecting certain groups; and (5) exclusion of children too ill to attend the schools where the examinations were made. The first four of these possible errors of survey technique we believe have been

From The California State Department of Public Health and The California Heart Association.

Received for publication April 24, 1944.

*The term "rheumatic fever" is used herein to include all recognized phases of the disease which are termed by some investigators, most notably Coburn, as the "rheumatic state." Further definition of this term will be given under the review of the criteria used for diagnosis. Rheumatic heart disease is the term applied to all positively diagnosed rheumatic, mitral, or aortic valvulitis which is not obviously associated with other congenital heart defects.

obviated. However, these surveys support the general belief that rheumatic fever is prevalent in temperate zones,[21, 22, 23] and especially in moderately high altitude areas such as Mexico City and the North Central Plains and Rocky Mountain Regions of the United States,[24] where extremes of temperature are common. Although the disease is uncommon in certain tropical and semitropical regions, such as the Caribbean Area and the Southern United States,[23, 25, 26] other localities in the tropical zones fail to show such immunity. These are most notably Ceylon,[27] Northern Australia,[28] and, judging from recent verbal reports of military officers, the islands in the tropical South Pacific area.

Insofar as some of the data in this paper support the suggestion, the disease has been thought to be more insidious in its onset in certain warmer climates, leaving in its wake unexplained valvulitis. There are considerable differences in the frequency of past histories of rheumatic fever among rheumatic cardiacs surveyed in different parts of this country.[23]

Fig. 1.—Map of California showing approximate location of towns of survey.

LOCALE FOR STUDY

The communities chosen for study were Eureka, Redlands, and Susanville; a brief description of each follows:

Eureka, the largest of the three towns, is the county seat of Humboldt County, and is located on Humboldt Bay on the Pacific Coast about 250

miles north of San Francisco. It is in "the heart of the Redwood Empire," and also in the center of a large dairy-farming region, so that its livelihood comes from lumbering, fishing, and agriculture. Redlands, the next largest, is an inland town in San Bernardino County about 80 miles southeast of Los Angeles. It is the center of a large navel-orange growing belt, and its prosperity fluctuates largely with the condition of the Eastern orange market. Susanville, the smallest town, is the county seat of Lassen County, and is in the center of a large pine-lumbering district. It is on the eastern slope of the Sierra Nevada Mountains, about 320 miles northeast of San Francisco and 85 miles northwest of Reno, Nevada.

CLIMATICOLOGIC DATA

The following tables show the variations in climatic data in the three towns over the four-year period of 1937, 1938, 1939, and 1940.

Table I gives the average annual mean temperature (degrees Fahrenheit), average total precipitation (in inches), average total snowfall

TABLE I

TOWN	COUNTY	ELEVATION (FT.)	TEMPERATURE (°F.)		PRECIPITATION (IN.)			NUMBER OF DAYS			
			LENGTH OF RECORD (YR.)	AVERAGE ANNUAL MEAN	LENGTH OF RECORD (YR.)	AVERAGE ANNUAL TOTAL	AVERAGE TOTAL SNOWFALL (UNMELTED)	CLEAR	PARTLY CLOUDY	CLOUDY	WITH PRECIPITATION 0.01 INCH OR MORE
Eureka	Humboldt	44	47	52.7	52	42.44	Tr	75	98	192	118
Redlands	San Bernardino	1352	48	62.6	52	17.10	0	264	64	37	46
Susanville	Lassen	4268	43	50.7	43	21.27	55.5	187	68	110	73

TABLE II

AVERAGE MEAN TEMPERATURE, BY MONTHS, FOR THE FOUR YEARS

TOWN	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	ANNUAL
Eureka	48.7	48.9	50.1	51.8	53.6	54.7	57.4	57.2	58.4	56.2	51.1	50.8	52.7
Redlands	48.9	49.7	54.3	60.3	64.8	70.3	75.7	76.4	73.3	65.4	57.1	54.9	62.6
Susanville	30.2	32.0	41.1	49.4	57.6	65.0	70.8	70.1	61.4	51.6	39.4	36.9	50.75

TABLE III

AVERAGE TOTAL PRECIPITATION, IN INCHES, BY MONTHS, FOR THE FOUR YEARS

TOWN	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	ANNUAL
Eureka	4.69	8.77	8.22	1.93	1.77	0.48	0.04	0.02	0.78	3.59	3.64	8.66	42.44
Redlands	2.52	3.91	3.86	1.44	0.23	0.01	0.02	0.00	0.87	0.56	0.58	3.10	17.10
Susanville	3.62	5.74	4.08	0.62	0.59	0.46	0.27	0.03	0.29	0.85	2.35	3.36	21.27

(unmelted), and average number of clear, partly cloudy, and cloudy days, and the average number of days with a precipitation of more than 0.01 inch for the year. It also gives the elevation of the town above sea level, and the length of record, i.e., number of years, that a weather station has been established in each town.

Table II gives the average mean temperature by months for the four-year period; Table III gives the average mean precipitation by months, snowfall not included, for the same years. Data for the mean relative humidity were not available for the three towns.

It can readily be seen from these tables that Eureka has a rather mild, constant temperature, but is quite damp, whereas Redlands may be considered as warm and fairly dry, with its rainfall coming in the winter months. Susanville has rather typical California "mountain climate"; it is quite cold in the winter, but hot in summer, and has only a moderate precipitation, most of which comes in the late winter and early spring.

DESCRIPTION OF POPULATION*

Eureka.—According to the 1940 census, the population of Eureka is 17,055 persons, consisting primarily of native-born whites of Scandinavian parentage, with a few Italians and Portuguese. There are no Chinese or Japanese, and only one or two Negro families.

TABLE IV

ECONOMIC INDEX OF TOWNS

TOWN	RETAIL TRADE 1939		WHOLESALE TRADE 1939		SERVICE ESTABLISHMENTS 1939				INCOME TAX RETURNS FILED 1938	
	NUMBER OF STORES	SALES ADD. 000	NUMBER OF ESTABLISHMENTS	NUMBER OF EMPLOYEES, AVERAGE FOR YEAR	TOTAL PAYROLL ADD. 000	NUMBER OF ESTABLISHMENTS	NUMBER OF EMPLOYEES, AVERAGE FOR YEAR	TOTAL PAYROLL ADD. 000	NUMBER	1940 POPULATION (%)
Eureka	390	11,749	46	219	328	165	169	174	1,442	8.45
Redlands	226	5,947	24	942	772	83	141	147	910	6.35
Lassen County*	208	5,631	18	58	93	44	62	70	341†	21.65

*Population, 14,479 (1940).

†Figure is for Susanville; it probably includes residents of County filing within City limits, but not living there.

Redlands.—The population of Redlands, by the 1940 census, is 14,324; the majority are whites, with a fair proportion of Mexicans, and a smaller group of Italians, Portuguese, and Negroes.

Susanville.—By the 1940 census, Susanville has 1,575 persons living within the city limits. The majority are whites, with a small percentage of Chinese and Negroes. The people are mostly of a stable, working

*There are no accurate figures on the population breakdown as to races, etc., according to the 1940 census. Those of 1930 are unreliable because of migration.

group, who derive their income primarily from the payrolls of the two lumber mills near the town.

After consulting various agencies,* no definite figures could be found on the socio-economic scale of living for the three towns, but Table IV might be of some interest and significance.

The figures in Table IV are not strictly comparable because Susanville is included with all of Lassen County. The large number of wholesale employees in Redlands are probably fruit packers and workers in the orange industry.

DESCRIPTION OF THE SCHOOL SYSTEMS

Eureka.—The school system consists of three public kindergartens; six public primary schools, first through sixth grades; one parochial school, kindergarten through eighth grades; one junior high school, grades 7, 8, and 9; and one Union Senior High School. The school population at the end of the 1940 school year was approximately as follows:

Public primary schools	1,432
Catholic parochial school	390
Junior high school	747
Senior high school	968
Total	3,537

The examinations were carried out in all but the seventh and eighth grades of the parochial school, so that all social and age groups were fully represented. A total of 2,703 pupils, or 76.6 per cent of the school population, were examined, plus thirty-four children of preschool age.

Redlands.—The school system consists of six public primary schools, kindergarten through sixth grades; one junior high school; one senior high school; and one parochial school. The exact distribution of the children in the various schools is not known, but the total public school population in June, 1939, was 3,669. During the spring of that year, 2,013 children were examined; a sample group was taken from all grades, with an approximately equal distribution for both age and social groups. In February and March, 1941, 562 new pupils in the kindergartens and first and fifth grades were examined, plus 177 pupils who had been in the 1939 group. These 177 were made up of 115 normal children who were re-examined in the fifth grade, and 62 out of 129 cardiac suspects who were found in the 1939 examinations and could still be in school in 1941. Roughly, then, 2,574 children were examined in 1939 and 1941 out of a total of approximately 4,223 pupils, or 60.8 per cent of the public school population.

Susanville.—The school system consists of four elementary schools, kindergarten through the eighth grade, and one combined Union High School and Junior College. The population of the elementary schools was 863 pupils at the close of the 1941 school year, whereas that of the

*California Department of Public Health, California Chamber of Commerce, California Medical Association, California Social Welfare Bureau, California Bureau of Labor Statistics, State Department of Epidemiology Statistics.

combined High School and Junior College was roughly 550 pupils. Because of local conditions and lack of time, examinations were carried out only in the elementary schools; a total of 838 pupils, or 97 per cent of the elementary school population, was examined. Thus this does not represent all age groups. All social groups were well represented.

PROCEDURE FOR THE SURVEY

The personnel for the survey consisted of: (1) a physician (Hahman), who carried out the examinations, read the roentgenograms and electrocardiograms, and made the diagnoses on all of the children; (2) a trained assistant, who took the height and weight measurements, brought the children to the examining room, and kept the records during the survey; and (3) a Public Health Nurse, assigned especially to the survey by the California State Department of Public Health, who made the home visits, assisted in taking the children to and from the roentgenographic laboratory, and, after training, took part of the histories.

The personnel was the same for all the surveys except that the work in Redlands, in 1939, was done by a second physician (Shearer), and the histories of the children in the Eureka Primary schools were not taken by the same Public Health Nurse who took those in the Eureka Junior and Senior High Schools and in the Redlands (1941) and Susanville schools.

The rest of the procedure, methods of examination, and criteria for diagnosis were the same for the three towns except for that part done in Redlands in 1939. The latter, however, closely paralleled those of the 1940 to 1941 survey, and the results, as far as the incidence of organic heart disease is concerned, are comparable.

The examinations of the children were carried out at the various schools in a relatively quiet, light, airy room which had been set aside for that purpose. Slips were sent by the schools to the parents for their consent for the physical examination, and, later, consent for laboratory study, that is, roentgenograms and electrocardiograms when necessary.

The time and date of the examinations were given to the parents, and their presence at the schools was encouraged. A complete history, with emphasis on facts pertaining to the etiological factors of rheumatic heart disease, and to the child's environmental conditions, was obtained for all the children examined. These histories were taken principally by the Public Health Nurse on her home visits, but, in about one-sixth of the cases, in Eureka especially, the histories were obtained from the parents at the time of the examination, or, in the older group, from the children themselves.

There was a small group of children that moved away from town after the examination, or whose parents refused to give the histories, and therefore those cases were discarded in tabulating the results of the survey.*

*Children confined at home were not included in the survey, and such cases, although rare, alter the sample of the population studied.

Fig. 2 is a sample form used for recording the histories and physical examination.

CARDIAC SURVEY

Town ---------- Date ---------- Schedule Number ----------
Name ---------- Age ---- Sex ---- Nationality ----------
Address ---------- Duration in town of survey ---- mo; ---- yr.
School ----------, grade ------; Religion ----------; Designate other localities and dates in which residence has been maintained since birth ------
---

Family history—cases cardiac or rheumatic state ----------
Personal history. Average hours sleep per day ----; adequate clothing ----------
Diet—milk ----, fruit ----, vegetables ----, protein ----, carbohydrates ----
Special comments ----------
General health—tonsil and adenoid infection ----------; frequent colds ----------; Dyspnea ------; fatigue ------; palpitation ------; sweats ------; history blue baby ------; other cardiac conditions ----------
Illness history (indicate age or year of occurrence and successive attacks)
Rheumatic fever --------; Rheum. pains { bone -------- / joint --------; Chorea -------- / muscle -------- }
Subq. nodules ----------; Nose bleeds ----------; Purpura ----------
Tonsillitis ----------; Otitis media ----------; Erythematous rash ----------
Scarlet fever --------; Diphtheria ----------; Other ----------

Home—No. rooms ----, No. sleeping rooms ----, No. with sunshine available ----
No. rooms with heat ----; type heating unit ----------; general sanitation----
----------; drainage on premises ----------

Physical examination—height ------; weight ------; temp. ------; nutrition standard -----; pallor -----; scoliosis -----; chest shape -----; throat inf. -----; dental caries ------; infection ------; lungs ------; lymph gl. cervical -----; heart apex. imp. ------ cm.; ------ mcl.; thrill --------
sounds—P_2---------- A_2---------- Murmurs ---------- Rate ----------
Rhythm ---------- Blood pressure R------ L------, B.P. legs------
Periph. vessels ----------

Fig. 2.

METHOD OF EXAMINATION

The children were brought to the examining room in groups of three or four of one sex, where they all stripped to the waist; large towels were given to the girls to drape over their shoulders. The height and weight measurements were then recorded, with the children's shoes left on to facilitate and speed the examination. When necessary, approximate deductions were made for boots and rubber or other heavy-soled shoes. Each child's nutrition was checked with the Faber "Weight-Height-Age Table for California School Children" (prepared for the San Francisco Tuberculosis Association),[29] which gives the normal height and weight range by sex for the ages of 5 to 15 years, inclusive. Any variation from the normal was recorded on the charts by the number of pounds above or below the normal figure for the given sex, age, and height.

The examiner sat with his back to a window, using only daylight for the examination, which was carried out as follows:

Inspection.—The examiner inspected the child in general to detect the presence or absence of pallor, cyanosis, scoliosis, or any marked chest

deformity. Absence was noted by an "O" sign; presence and its degree of severity by the plus sign and its multiple. Any chest deformity was described, and the degree of severity noted as mild, moderate, or severe.

The mouth and throat were then inspected, with the aid of a tongue blade, for the presence of caries, mouth infection, and particularly throat infection and tonsillar enlargement. Any variations from normal were again recorded by the signs "one, two, or three plus" as follows: (1) *Dental caries*, +, one or two teeth with small cavities; ++, at least two teeth with moderately large cavities, or three or four with small cavities; and +++, four or more teeth with cavities of moderate size, or three or four with huge cavities. (2) *Throat infection* +, red, inflamed fauces, tonsils out or not appreciably enlarged; ++, almond- to chestnut-sized tonsils without evident infection; +++, above size with evident infection, or huge tonsils that filled the posterior pharynx.

Palpation.—(1) Palpation of the neck was used to detect any enlargement of the cervical lymph nodes. (2) Palpation of the chest was used to detect the presence of a thrill and to locate the point of maximum apical impulse (PMI). The distance of the PMI and midclavicular line from the midsternal line was then measured with a centimeter rule, the measurements recorded, and a comparison of the two was used as an indication of the heart size. If the midclavicular point was not less than the distance of the PMI from the midsternal line, the heart was considered to be of normal size. Displacement of the heart, as by scoliosis, was evaluated.

Percussion.—Percussion was used only when a child was suspected of having a lung disease or heart enlargement, as noted by the position of the PMI.

Auscultation.—(1) Auscultation of the lungs was used to ascertain the presence or absence of "squeaks," râles, or rubs, and (2) of the heart, in the standing and supine positions, to ascertain the cardiac rate and rhythm, the quality and intensity of the heart sounds, and the presence of murmurs or other abnormal sounds. The rate was counted in all cases while the patient was lying on the examining table; the auscultatory method was used, and the number of apical beats was counted for at least a fifteen-second interval.

Any child suspected of having heart disease was also examined after exercise, which consisted of jumping up and down fifteen to twenty times on each foot, and in the sitting and left lateral positions. A notation was also made of the presence of any abnormal sounds over the peripheral vessels.

The blood pressure was taken on all the children in the supine position at the conclusion of the examination. A 12 cm. cuff was used on the right arm, and was found to be of satisfactory size for all but the smaller children, of 5 years or under, and for the markedly obese of 14 years or older. In any case in which disease was suspected, the pressure was also taken on the left arm, and on the legs when necessary. Any child with a brachial systolic blood pressure greater than 140 mm. Hg, without obvious signs of undue nervousness, was brought back at a later date, when possible, and the pressure retaken.

Any child who was found to have signs of an organic heart lesion, but who had a negative history of rheumatic fever, and in whom the diagnosis was not certain, was brought back for re-examination at a later date. If the diagnosis was still doubtful, roentgenograms and electrocardiograms were made when possible; this work was done at the

offices of the local radiologists. Electrocardiograms were not taken on the small group of Redlands children (eleven) who were sent for roentgenograms in the 1940 survey (Hahman).

CRITERIA FOR DIAGNOSIS

The following definitions were used in the diagnosis and classification of the various murmurs or conditions found during the survey.

1. *Normal.*—Any child without a history of rheumatic fever, rheumatic joint, bone, or muscle pains (so-called "growing pains") or chorea, and with no heart murmur at the time of the examination was classified as "normal."

2. *Functional.*—Any child with a soft systolic murmur over the precordium that varied with respirations and change of position, became louder after exercise, and was not transmitted to the back, neck, or axilla was classified as "functional." This diagnosis was also used in those cases in which there was a marked variation in the murmurs as heard during the first examination and as heard again at the time of the recheck. No attempt was made to segregate the so-called "accidental" and "cardiorespiratory" murmurs from the "functional" murmurs due to anemia, recent fever, or other possible cause. "Functional," therefore, as used in this survey, denotes those murmurs which were thought definitely to be "nonorganic" in the broadest sense of the term, as opposed to the "organic" murmurs of congenital or rheumatic origin which, we presuppose, are associated with definite, and probably permanent, vascular, myocardial, or valvular deformity.

3. *Potential Rheumatic* (rheumatic fever without evident heart disease).—In this group were those cases in which there was a history of one of the primary manifestations of rheumatic fever, namely, acute polyarthritis, chorea, or recurrent bone, joint, or muscle pains, but without any evidence of organic heart disease or active infection at the time of the examination.

4. *Rheumatic Fever History.*—Cases in which there was a history of one of the primary rheumatic manifestations, or a history of two or more of the secondary manifestations, e.g., recurrent tonsillitis or torticollis, purpura, frequent, unexplained, severe epistaxis, various erythemata, and subcutaneous nodules were included in this group.

a. With valvulitis: Definite evidence of one or more of the following: aortic insufficiency and/or stenosis, mitral insufficiency and/or stenosis (pulmonary and tricuspid valvular lesions not to be considered rheumatic in absence of mitral valve lesions).

b. With probable heart disease: Myocarditis with above criteria for rheumatic fever.

5. *Mitral and/or Aortic Valvulitis.*—This group did not include cases of congenital or syphilitic heart disease.

a. Rheumatic heart disease without a rheumatic fever history. Cases in which there were signs of mitral or aortic valvulitis without any known history of previous infection.

b. With scarlet fever history: Cases in which there were signs of valvulitis, as previously mentioned, without history of rheumatic infection, but with definite history of scarlet fever at some time prior to the date of examination or prior to the discovery of a murmur by a local physician.

6. *Congenital Heart Disease.*—This group included those cases in which there were characteristic physical signs, with confirmation by roentgenogram and electrocardiogram.

7. *Hypertension.*—This diagnosis denotes probably only a transient affair, and cannot be considered as true hypertension in all cases. Using the reports of Faber and James,[30] Taussig and Hecht,[31] and others, the maximal blood pressures for given age groups were set as follows: (a) 5 to 9 years, inclusive, 120/80; (b) 10 to 14 years, inclusive, 130/85; and (c) 15 years and over, 140/90.

Whenever a diagnosis of hypertension was then made, it was classed as an incidental finding, and not as the primary diagnosis.

8. *Unclassified Group* (classification unknown).—In this group were those cases in which there was no history of rheumatic fever, but in which there were murmurs which did not definitely fit any of the above criteria, and in which the roentgenograms and electrocardiograms were normal or of no diagnostic value. According to the type, quality, and location of the murmur, the cases were classified as follows: (a) rheumatic vs. functional, (b) congenital vs. functional, and (c) rheumatic vs. congenital.

Certain cases of organic heart disease undoubtedly are included in this group.

9. *Positive Family History.*—Those cases in which there was a history of rheumatic fever or chorea, or rheumatic heart disease in the immediate family or in some person or relative in intimate daily contact with the patient were classified as having "positive family history." This was also an incidental diagnosis, and is classed with one of the previously mentioned primary diagnoses.

The data obtained from the histories and physical examinations were assembled by the Statistical Division of the California State Department of Public Health in five sets of tables, twelve to a set. The sets were for: (1) The Shearer Redlands Survey of 1940; (2), (3), and (4) The Hahman Surveys of Redlands, Eureka, and Susanville of 1940 and 1941; and (5) the total of the Hahman surveys. The titles of the original tables of each set were:

Table I, "Showing Distribution and Percentage by Diagnosis;" Table II, "Showing Distribution and Percentage by Age and Diagnosis;" Table III, "Showing Distribution and Percentage by Sex and Diagnosis;" Table IV, "Showing Distribution and Percentage by Race and Diagnosis;" Table V, "Distribution and Percentage of Those With a Positive Family History in Each Diagnostic Group;" Table VI, "Distribution and Percentage of Diagnostic Groups According to Food Consumption;" Table VII, "Evaluation of Housing Conditions, Showing Distribution and Percentage for each Diagnostic Group;" Table VII-A, "Evaluation of Housing Conditions Based on Crowding Alone, Showing Distribution and Percentage for Each Diagnostic Group;" Table VIII, "Distribution and Percentage of Hypertension in Diagnostic Groups;" Table IX, "Distribution and Percentage of Selected Points of Physical Examination for Each Diagnostic Group;" Table X, "Distribution and Percentage of Nutritional Standards by Diagnostic Group;" Table XI, "Distribution and Percentage of Certain Organic Troubles by Diagnostic Group;" Table XII, "Frequency of Upper Respiratory Infections and Incidence of Various Diseases by Diagnosis."

DISCUSSION OF DATA

The data from some of these tables have been reorganized, and the following constitutes a discussion of the material contained in these revised tables. In reproduction of tables, the letters "S" and "H" indicate Shearer or Hahman as the surveyor.

Tables V and VI present the total figures for the entire survey, and show the comparison of the "S" and "H" studies and the effect of exclusion of 447 cases in which there were no histories or no established residence of over two years in the community. The results of the grand total are chiefly important in the number of congenital heart lesions and functional murmurs, for those figures are probably not influenced by residence or inadequate histories in Table VII. Since the method of history taking was faulty in the 1939 Redlands "S" survey, all of the figures on the "S" survey are to be discounted where history is concerned, as in "Potential Rheumatic Heart Disease," or "Rheumatic History in Cases of Rheumatic Heart Disease."

The incidence of 0.7 per cent of congenital heart disease is comparable with the 0.65 per cent found after exclusion of the 447 cases mentioned. This is a high incidence when compared to many previous surveys, but is not greatly different from that found by Sampson, Christie, and Geiger,[17] in San Francisco, in 1938.

The incidence of 16.6 per cent of functional murmurs may seem to be low. The incidence of rheumatic heart disease and total rheumatic cases of 1.3 per cent and 1.9 per cent, respectively, is unusually high for what has been considered an area in which endemic rheumatic disease is rare. As is shown in Tables VIII and IX, this is due to the fact that a larger population was examined in Eureka and Susanville, which together somewhat exceed Redlands. The figures of 1.17 per cent rheumatic heart disease and 1.7 per cent total rheumatic heart disease, as obtained from the entire series after exclusion of the 447 cases, probably indicate more accurately the actual incidence of these conditions. Likewise, the percentage of congenital heart disease is more accurately indicated by 0.65 per cent, and of total organic heart disease by 1.82 per cent.

The data presented in Table VI indicate that care must be exercised in reporting local surveys to exclude cases in which rheumatic disease may have been acquired elsewhere.

Table VII, a summary of the Redlands surveys, shows a fair agreement between the "S" and "H" reports in the incidence of congenital heart disease, but a considerable disagreement in the percentage of rheumatic potential and actual heart disease. This can probably be explained in three ways: (1) differences in personal interpretation of observations; (2) selection of only certain school grades in the "H" study; and (3) "chance" in dealing with such small figures, i.e., only ten rheumatic cases in the "S" survey and five in the "H" survey.

In spite of these differences, the total figure of 0.19 per cent potential, and 0.38 per cent rheumatic, heart disease, and 0.57 per cent total rheumatics is a significantly low incidence. This is as may be expected in the warm, dry climate of Redlands.

In reference to Susanville, Table VIII, the population was smaller, and, therefore, the figures are more subject to statistical misinterpreta-

TABLE V

SUMMARY OF 1939 AND 1940 TO 1941 SURVEYS IN REDLANDS, EUREKA, AND SUSANVILLE, CALIFORNIA

		TOTAL	NORMAL WITHOUT MURMUR	NORMAL WITH FUNCTIONAL MURMUR	NORMAL TOTAL	UNCLASSIFIED	CONGENITAL HEART DISEASE	POTENTIAL RHEUMATIC HEART DISEASE	RHEUMATIC HEART DISEASE	TOTAL RHEUMATIC CASES		TOTAL ORGANIC HEART DISEASE
										RHEUMATIC HISTORY		
										POS.	NEG.	
All children examined, including Redlands 1939 "S" survey and 447 cases of Table VI; Redlands (2,698), Eureka (2,719), and Susanville (832)	Number of cases	6,249	4,972	1,036	6,008	77	43	38	81		119	124
	Percentage	100	79.5	16.6	96.1	1.2	.7–	.6+	1.3		1.9	2
1939 "S" survey of Redlands (2,012) and 1940 to 1941 "H" survey of Redlands (686), Eureka (2,719), and Susanville (832); *excluding* 447 cases of Table VI	Number of cases	5,802	4,664	938	5,602	64	38	30	68		98	106
	Percentage	100	80	16.1	96.1	1.1	.65	.52	1.17		1.7	1.82
1940 to 1941 "H" survey of Redlands, Eureka, and Susanville	Number of cases	3,790	2,779	835	3,614	63	25	26	62	22	40	88	87
	Percentage	100	73	22	95	1.66	.66	.68	1.63	.58	1.06	2.32	2.29

TABLE VI

ANALYSIS OF 447 CASES EXCLUDED FROM TABLE V

	TOTAL NUMBER CASES	NORMAL WITHOUT MURMUR	NORMAL WITH FUNCTIONAL MURMUR	NORMAL TOTAL	UNCLASSIFIED	CONGENITAL HEART DISEASE	POTENTIAL RHEUMATIC HEART DISEASE	RHEUMATIC HEART DISEASE	TOTAL RHEUMATIC CASES	TOTAL ORGANIC HEART DISEASE
Length of residence unknown	11	5	5	10	1	-	-	-	-	-
Residence less than two years	406	303	87	390	4	5	3	4	7	9
Rheumatic illness not contacted in area	14	-	-	-	-	-	5	9	14	9
Examined but history refused	16	-	16	16	-	-	-	-	-	-
Total cases	447	308	108	416	5	5	8	13	21	18
Percentage	100	69	24.3	93	1.1	1.1	1.8	2.9	4.7	4

TABLE VII

SUMMARY OF 1939 (S) AND 1940 TO 1941 (H) SURVEYS OF 2,663 CHILDREN IN REDLANDS

	TOTAL	NORMAL WITHOUT MURMUR	NORMAL WITH FUNCTIONAL MURMUR	NORMAL TOTAL	UNCLASSIFIED	CONGENITAL HEART DISEASE	POTENTIAL RHEUMATIC HEART DISEASE	RHEUMATIC HEART DISEASE			TOTAL RHEUMATIC CASES	TOTAL ORGANIC HEART DISEASE
1939 (S) Redlands												
Number of cases	2,012	1,885	103	1,988	4	13	4	6			10	19
Percentage	100	93.6–	5.1	98.7–	.2	.64	.2	.3			.5	.94
1940 to 1941 (H) Redlands									RHEUMATIC HISTORY POS.	NEG.		
Number of cases	621	492	114	606	5	5	1	4	1	3	5	9
Percentage	100	79	18.3	97.3	.8	.8	.16	.65	.16	.48	.8	1.45
Total	2,633	2,377	217	2,504	9	18	5	10			15	28
Percentage	100	90.5	8.2	98.7	.34	.76	.19	.38			.57	1.14

tion. This is especially so with congenital heart disease, with only three cases and a percentage incidence of 0.4 per cent, about two-thirds of the incidence of the whole group. The high frequency of rheumatic fever (including rheumatic heart disease), and rheumatic heart disease, namely, 2.6 per cent and 1.1 per cent, seems to be significant statistically. This community has a climate not unlike the high altitude communities of Salt Lake City and Denver, both of which are now known to have high rheumatic fever morbidity and mortality rates.

Eureka, Table IX, with its remarkably uniform, cool, damp climate, presents the highest incidence of rheumatic heart disease (2.0 per cent), although the less dependable figures of potential rheumatic heart disease and total rheumatic disease are respectively lower and equal to those of Susanville. Congenital heart lesions were nearly as frequent as in Redlands, 0.7 per cent (0.69+ per cent) compared to 0.76 per cent. Inasmuch as housing projects were under construction in Eureka and a general im-

TABLE VIII

SHOWING DISTRIBUTION AND PERCENTAGE BY DIAGNOSIS OF 732 CHILDREN IN SUSANVILLE*

	TOTAL	NORMAL WITHOUT MURMUR	NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER	NORMAL WITH FUNCTIONAL MURMUR	TOTAL NORMAL	UNCLASSIFIED	CONGENITAL HEART DISEASE	POTENTIAL RHEUMATIC HEART DISEASE	RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER	RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER	TOTAL RHEUMATIC HEART DISEASE	TOTAL RHEUMATIC DISEASE	TOTAL ORGANIC HEART DISEASE
Number	732	541	27	136	704	6	3	11	4	4	8	19	11
Percentage	100	73	3.7	18.6	95.3	0.8	0.4	1.5	0.5	0.5	1.1	2.6	1.5

*One hundred additional children were examined, but were excluded from this table because of residence of less than two years or because rheumatic fever was contracted elsewhere.

TABLE IX

SHOWING DISTRIBUTION AND PERCENTAGE BY DIAGNOSIS OF 2,450 CHILDREN IN EUREKA*

TOTAL	NORMAL WITHOUT MURMUR	NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER	NORMAL WITH FUNCTIONAL MURMUR	TOTAL NORMAL	UNCLASSIFIED	CONGENITAL HEART DISEASE	POTENTIAL RHEUMATIC HEART DISEASE	RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER	RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER	TOTAL RHEUMATIC HEART DISEASE	TOTAL RHEUMATIC DISEASE	TOTAL ORGANIC HEART DISEASE
2450	1662	57	585	2304	52	17	14	33	17	50	64	67
100	68	2.3	23.8	94.2	2.1	0.7	0.6	1.3	0.7	2	2.6	2.7

*One hundred additional children were examined, but were not included because of residence of less than two years, or because rheumatic fever was contracted elsewhere, or because of inadequate history.

provement in living standards was occurring, a repetition of the survey in this city in five to ten years may show the influence of such social changes in the rheumatic disease incidence. All sets of tables are being retained for such possible comparison in future studies.

The report of a positive history of rheumatic fever in any of its manifestations occurred in 35 per cent of all cases of rheumatic heart disease, in 25 per cent of the Redlands cases ("H" survey), 50 per cent of the Susanville cases, and 35 per cent of the Eureka cases. With the exception of the Susanville report, these are lower figures than have been published previously in most surveys.[32, 33]

Tables X to XV deal with certain data on the consolidated reports of all three communities surveyed by Hahman. Similar tables, as previously stated, are available for each individual town, but their comparison was not considered of sufficient importance to be presented here.

Table X confirms more recent reports[11] that older males are affected with rheumatic disease more frequently than females, i.e., 61.4 per cent and 38.6 per cent, respectively. This is particularly evident in the group with rheumatic heart disease without a rheumatic history.

Table XI, on relation of race to rheumatic disease, shows how largely the population was composed of whites; the very few Negroes and most of the Mexicans were concentrated in Southern California (Redlands). As has been previously reported by Paul and Dixon,[34] the incidence of rheumatic disease in Indians living in northern temperate zones is high, and this was found in our survey; 4.6 per cent of the total rheumatic population was Indian, compared to 2.1 per cent of the normal population. Thus, 5 per cent of the whole Indian population had rheumatic disease, and 3.3 per cent had rheumatic heart disease. Mexicans did not seem to be especially susceptible, although the figures for Redlands, not given in a table, were 1 per cent of rheumatic disease in Mexicans, as contrasted to 0.57 per cent in the entire population. The number of cases in both of these racial groups is too small to draw any positive conclusion. The observations should be considered as only suggestive.

Table XII is presented to illustrate how infrequently a family history of rheumatic fever or rheumatic heart disease was obtained in this survey. Only 5.7 per cent of rheumatic children gave a positive family history, which was hardly a significant difference from the 3.6 per cent rheumatic family histories in the normal group. Reasonable care was exercised in obtaining family histories from parents, but the low figures, when compared to other reports,[35] throw some doubt on the accuracy of these histories.

Table XIII shows the effect of housing,* and of crowding, in particular, on the occurrence of rheumatic disease.[36-38] There was a recog-

*Housing:

Good—1 or less person per room, and heat in over half of the rooms of the house: i.e., three rooms in a five-room house.

Fair—1 to 1½ persons per room, with heat in more than half of the rooms of the house.

Poor—More than 1½ persons per room, or 1 to 1½ persons per room, with heat in one-half the house or less.

TABLE X

SHOWING DISTRIBUTION AND PERCENTAGE BY SEX AND DIAGNOSIS
Total of 3,790 Cases, 1940 to 1941 Surveys (H)

SEX	TOTAL		NORMAL WITHOUT MURMUR		NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER		NORMAL WITH FUNCTIONAL MURMUR		TOTAL NORMAL		UNCLASSIFIED		CONGENITAL HEART DISEASE		POTENTIAL RHEUMATIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER		RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER		TOTAL RHEUMATIC DISEASE	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Male	1,891	49.9	1,326	49.5	52	55.3	407	48.7	1,783	49.5	40	63.5	12	48.0	15	57.7	27	67.5	12	54.5	54	61.4
Female	1,899	50.1	1,359	50.5	42	44.7	428	51.3	1,831	50.5	23	36.5	13	52.0	11	42.3	13	32.5	10	45.5	34	38.6
Total	3,790	100.0	2,685	100.0	94	100.0	835	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0

TABLE XI

SHOWING DISTRIBUTION AND PERCENTAGE BY RACE AND DIAGNOSIS
Total of 3,790 Cases, 1940 to 1941 Surveys (H)

RACE	TOTAL		NORMAL WITHOUT MURMUR		NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER		NORMAL WITH FUNCTIONAL MURMUR		TOTAL NORMAL		CONGENITAL HEART DISEASE		POTENTIAL RHEUMATIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER		RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER		TOTAL RHEUMATIC DISEASE		UNCLASSIFIED	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
White	3,396	89.6	2,389	89.0	88	93.6	756	90.5	3,233	89.5	23	92.0	24	92.4	38	95.0	19	86.4	81	92.0	59	93.6
Indian	82	2.2	60	2.2	3	3.2	13	1.6	76	2.1+	-	-	1	3.8	1	2.5	2	9.1	4	4.6	2	3.2
Negro	20	0.5	17	0.6	-	-	3	0.4	20	.55	-	-	-	-	-	-	-	-	-	-	-	-
Mexican	246*	6.5	186	6.9	1	1.1	52	6.2	239	6.64	2	8.0	1	3.8	1	2.5	1	4.5	3	3.4	2	3.2
Filipino	1	0.0	1	0.1	-	-	-	-	1	.02	-	-	-	-	-	-	-	-	-	-	-	-
Oriental	6	0.2	4	0.1	-	-	2	0.2	6	.17	-	-	-	-	-	-	-	-	-	-	-	-
Unknown	39	1.0	28	1.1	2	2.1	9	1.1	39	1.1	-	-	-	-	-	-	-	-	-	-	-	-
Total	3,790	100.0	2,685	100.0	94	100.0	835	100.0	3,614	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0	63	100.0

Two hundred nineteen of these cases were from Redlands and constituted 35.3 per cent of the total number examined in that city. In the remaining thirty-three Mexican children only one case of organic heart disease was found and a "rheumatic without history."

TABLE XII

DISTRIBUTION AND PERCENTAGE OF THOSE WITH A POSITIVE FAMILY HISTORY OF RHEUMATIC FEVER IN EACH DIAGNOSTIC GROUP
Total of 3,790 Cases, 1940 to 1941 Surveys (H)

	TOTAL		NORMAL WITHOUT MURMUR		NORMAL WITH FUNCTIONAL MURMUR		TOTAL NORMALS		UNCLASSIFIED		CONGENITAL HEART DISEASE		POTENTIAL RHEUMALTIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY OR RHEUMATIC FEVER		RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER		TOTAL RHEUMATIC DISEASE	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
With positive family history of rheumatic fever	139	3.7	94	3.4	35	4.2	129	3.6	4	6.3	1	4.0	1	3.8	2	5.0	2	9.1	5	5.7
Without positive family history of rheumatic fever	3,651	96.3	2,685	96.6	800	95.8	3,485	96.4	59	93.7	24	96.0	25	96.2	38	95.0	20	90.9	83	94.3
Total	3,790	100.0	2,779	100.0	835	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0

TABLE XIII

EVALUATION OF HOUSING CONDITIONS, SHOWING DISTRIBUTION AND PERCENTAGE FOR EACH DIAGNOSTIC GROUP
Total of 3,790 Cases, 1940 to 1941 Surveys (H)

HOUSING EVALUATION	TOTAL		NORMAL WITHOUT MURMUR		NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER		NORMAL WITH FUNCTIONAL MURMUR		TOTAL NORMAL		UNCLASSIFIED		CONGENITAL HEART DISEASE		POTENTIAL RHEUMATIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY		RHEUMATIC HEART DISEASE WITH HISTORY		TOTAL RHEUMATIC	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Poor	736	19.4	529	19.7	20	21.3	157	18.8	706	19.5	8	12.7	6	24.0	3	11.5	8	20.0	5	22.7	16	18.2
Fair	1,484	39.2	994	37.0	42	44.7	354	42.4	1,390	38.5	35	55.6	10	40.0	15	57.7	20	50.0	14	63.6	49	55.7
Good	1,570	41.4	1,162	43.3	32	34.0	324	38.8	1,518	42.0	20	31.7	9	36.0	8	30.8	12	30.0	3	13.7	23	26.1
Total	3,790	100.0	2,685	100.0	94	100.0	835	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0
1 or less per room	2,659	70.2	1,881	70.1	57	60.6	595	71.2	2,533	70.+	51	81.0	18	72.0	20	77.0	28	70.0	9	40.9	57	64.8
More than 1, less than 1½	588	15.5	414	15.4	24	25.6	120	14.4	558	15.4	6	9.5	3	12.0	3	11.5	10	25.0	8	36.4	21	23.9
1½ or more per room	543	14.3	390	14.5	13	13.8	120	14.4	523	14.5	6	9.5	4	16.0	3	11.5	2	5.0	5	22.7	10	11.3

TABLE XIV

DISTRIBUTION AND PERCENTAGE OF CERTAIN SIGNS AND SYMPTOMS OF ORGANIC TROUBLES BY DIAGNOSTIC GROUP
Total of 3,790 Cases, 1940 to 1941 Surveys (H)

	TOTAL		NORMAL WITHOUT MURMUR		NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER		NORMAL WITH FUNCTIONAL MURMUR		TOTAL NORMAL		UNCLASSIFIED		CONGENITAL HEART DISEASE		POTENTIAL RHEUMATIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER		RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER		TOTAL RHEUMATIC CASES	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Dyspnea	32	0.8	11	0.4	1	1.1	13	1.6	25	0.7	2	3.2	–	–	2	7.7	1	2.5	2	9.1	5	5.7
Fatigue	425	11.2	269	10.0	12	12.8	107	12.8	388	10.7	8	12.7	10	40.0	5	19.2	6	15.0	8	36.4	19	21.6
Palpitation	91	2.4	41	1.5	2	2.1	27	3.2	70	2.1	4	6.3	6	24.0	1	3.8	5	12.5	5	22.7	11	12.5
Sweats	66	1.7	31	1.2	1	1.1	21	2.5	53	1.46	2	3.2	2	8.0	1	3.8	4	10.0	4	18.2	9	10.2
Blue baby	24	0.6	8	0.3	1	1.1	9	1.1	18	0.5	2	3.2	2	8.0	–	–	–	–	2	9.1	2	2.3
Other cardiac signs and symptoms	75	2.0	30	1.1	1	1.1	25	3.0	56	1.5	5	7.9	7	28.0	1	3.8	1	2.5	5	22.7	7	8.0
None given	3,225	85.1	2,350	7.5	79	84.0	686	82.2	3,115	86.2	46	73.0	12	48.0	16	61.5	29	72.5	7	31.8	52	59.1
Total cases examined*	3,790	100.0	2,685	100.0	94	100.0	835	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0

*The total of the vertical columns does not agree with the total number of children examined because of occurrence of multiple symptoms in certain patients.

nizable concentration of the rheumatic population in houses evaluated as fair, 55.7 per cent, as compared to 38.5 per cent of the normal subjects. This is not shown in poor housing, although, when poor and fair housing are consolidated and contrasted to good housing, there is a material difference, i.e., 74 per cent in rheumatics and 58 per cent in normals. A similar situation obtains in the apparent effect of the crowding element of housing, but is less evident than in the general housing classification, i.e., 35.2 per cent of the rheumatic group and 30 per cent of the normal population were living in houses with more than one person per room.

Table XIV summarizes the history of certain common cardiac signs and symptoms. More extensive tables of phenomena associated with heart disease and rheumatism were prepared, but are not presented because the data contained did not seem significant. With the exception of fatigue, the source of which is manifold, no other signs or symptoms were reported in consequential number among normal children.

Dyspnea, fatigue, palpitation, and excessive sweating were relatively common in the rheumatic population. Unusual dyspnea on exertion may have been due to poor training after confinement to bed or limited activity, rather than heart failure. This would explain its relative infrequency in "rheumatic heart disease without history," as compared to those patients with and without heart disease but with a history of rheumatic fever. Palpitation was relatively frequent only among children with heart disease. The occurrence of two blue babies at birth, reported as rheumatic heart disease, only indicates that this historical finding is often unreliable.

Table XV presents the age distribution of the children studied. As would be expected, and as in the San Francisco[17] and other surveys, congenital heart lesions are more common than rheumatic valvulitis prior to the age of 9 years. It is recognized through several surveys that the greatest number of children with rheumatic disease have their initial attack between 10 and 16 years of age. One would assume that more children would be found with evidence of rheumatic heart disease over this age than under it. Although this was the situation in a previous San Francisco study, it is not uniformly the case, nor was it found in the current study.

Presenting the data in a different way than in the table, it is found that, from the ages of 5 through 9 years, 2.9 per cent of the population had rheumatic disease and 0.8+ per cent had valvulitis. From the ages of 10 through 14 years, the incidences were 3.3 per cent and 2.4 per cent, respectively, and from 15 through 19 years, 3.4 per cent and 1.7 per cent. The fact that there is a lower incidence of rheumatic heart disease in late youth has been frequently reported. The accepted explanation is that signs of valvulitis are evanescent, and are transiently lost in the adolescent and postadolescent period.

Table XVI does not show a high incidence of rheumatic disease in the lower dietary brackets. The diet history for special elements was

TABLE XV

SHOWING DISTRIBUTION AND PERCENTAGE BY AGE AND DIAGNOSIS

Total of 3,790 Cases of 1940 to 1941 Surveys (H)

AGE (YR.)	TOTAL		NORMAL WITHOUT MURMUR		NORMAL WITH FAMILY HISTORY OF RHEUMATIC FEVER		NORMAL WITH FUNCTIONAL MURMUR		TOTAL NORMAL		UNCLASSIFIED		CONGENITAL HEART DISEASE		POTENTIAL RHEUMATIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER		RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER		TOTAL RHEUMATIC CASES		PERCENTAGE OF EACH AGE GROUP			
																							TOTAL RHEUMATIC DISEASE	RHEUMATIC HEART DISEASE	CONGENITAL HEART DISEASE	TOTAL HEART DISEASE
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%				
0 to 4	21	0.6	14	0.5	1	1.1	4	0.4	19	5.0	–	–	2	8.0	–	–	–	–	–	–	–	–	–	–	9.5	9.5
5 to 9	1,550	40.9	1,099	40.9	43	45.7	343	41.1	1,485	41.5	31	49.2	14	56.0	7	26.9	9	22.5	4	18.2	20	22.7	2.9-	0.83	0.91	1.74
10 to 14	1,520	40.1	1,050	39.1	43	45.7	343	41.1	1,436	40.4	26	41.3	7	28.0	14	53.9	24	60.0	13	59.1	51	58.0	3.3	2.43	0.46-	2.89
15 to 19	696	18.4	519	19.3	7	7.5	145	17.4	671	18.5	6	9.5	2	8.0	5	19.2	7	17.5	5	22.7	17	19.3	2.4	1.71	0.29-	2.0
20+	2	0.0	2	0.1	–	–	–	–	2	0.05	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Unknown	1	0.0	1	0.1	–	–	–	–	1	0.03	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Total	3,790	100.0	2,685	100.0	94	100.0	835	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0	2.32	1.63	0.66	2.29

TABLE XVI

DISTRIBUTION AND PERCENTAGE OF DIAGNOSTIC GROUPS ACCORDING TO FOOD CONSUMPTION AND INCIDENCE OF MARKED DENTAL CARIES
3,790 Cases of 1940 to 1941 Survey (H)

		TOTAL		TOTAL NORMAL		UN-CLASSIFIED		CONGENITAL HEART DISEASE		POTENTIAL RHEUMATIC HEART DISEASE		RHEUMATIC HEART DISEASE WITHOUT HISTORY OF RHEUMATIC FEVER		RHEUMATIC HEART DISEASE WITH HISTORY OF RHEUMATIC FEVER		TOTAL RHEUMATIC DISEASE		DENTAL CARIES	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
General diet	+	536	14.2	512	14.2	8	12.7	3	12.0	2	7.7	6	15.0	5	22.7	13	14.8	–	–
	++	871	23.0	829	22.8+	15	23.8	11	44.0	6	23.1	6	15.0	4	18.2	16	18.2	–	–
	+++	1,335	35.2	1,266	35.0+	26	41.3	8	32.0	10	38.4	14	35.0	11	50.0	35	39.8	–	–
	++++	1,048	27.6	1,007	28.1	14	22.2	3	12.0	8	30.8	14	35.0	2	9.1	24	27.2	–	–
	Total	3,790	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0	–	–
Vitamin C	+	138	3.6	123	3.4	9	14.3	–	–	1	3.8	3	7.5	2	9.1	6	6.8	–	–
	++	298	7.9	277	7.6	6	9.5	4	16.0	2	7.7	5	12.5	4	18.1	11	12.5	–	–
	+++	1,179	31.1	1,108	30.6	28	44.4	11	44.0	5	19.2	19	47.5	8	36.4	32	36.4	–	–
	++++	2,175	57.4	2,106	58.5	20	31.8	10	40.0	18	69.3	13	32.5	8	36.4	39	44.3	–	–
	Total	3,790	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0	–	–
Carbohydrates	+	55	1.4	53	1.5	2	3.2	–	–	–	–	–	–	–	–	–	–	8	1.3
	++	771	20.3	738	20.4	11	17.4	6	24.0	2	7.7	11	27.5	3	13.6	16	18.2	102	16.7
	+++	1,712	45.2	1,611	44.6	41	65.1	9	36.0	18	69.3	18	45.0	15	68.2	51	58.0	253	41.5
	++++	867	22.9	840	23.0	7	11.1	6	24.0	5	19.2	5	12.5	4	18.2	14	15.9	129	21.1
	+++++	385	10.2	372	10.6	2	3.2	4	16.0	1	3.8	6	15.0	–	–	7	7.9	118	19.4
	Total	3,790	100.0	3,614	100.0	63	100.0	25	100.0	26	100.0	40	100.0	22	100.0	88	100.0	610	100.0
Dental caries		610	100.0	580	95.0	9	1.5	7	1.1	4	0.7	7	1.1	3	0.5	14	2.3	610	100.0

not obtained except for vitamin C and carbohydrate content. Rinehart and Mettier, in 1934,[39] and later, with other collaborators,[40] presented evidence that rheumatic fever was a result of latent scurvy with superimposed infection. This view was partially corroborated by Stimson, Hedley, and Rose,[41] but Sendroy and Schultz[42] and Perry[43] failed to find confirmatory evidence of any specific relation of vitamin C deficiency and rheumatic fever.

In the Redlands survey (H), all five rheumatic children had been using adequate amounts of citrus fruits (groups +++ and ++++). However, in Table XVI the rheumatic population seems to be concentrated in lower brackets of vitamin C intake. This may suggest a contributory, rather than a required, causative relation of vitamin C intake and rheumatic fever.

The carbohydrate study was largely to ascertain the relation to dental caries. Only in the ++++ bracket was there an apparent correlation. There was no greater incidence of dental caries in rheumatic than in normal children, 15.9 per cent and 16.3 per cent, respectively.

There was no correlation of rheumatic disease with malnutrition, or with a history of frequent throat infections or of appreciable cervical lymphadenopathy.

Of rheumatic children, 11.4 per cent had had scarlet fever, as contrasted to 8.9 per cent of normal children, but no data were available as to the interval between the scarlet fever and the rheumatic fever. These figures, therefore, are not significant.

Of the rheumatic children, 41 per cent had had their tonsils and adenoids removed, as contrasted with 36 per cent of normal children, but there was no history available on the development or exacerbation of rheumatic fever in relation to the time the tonsillectomy was performed. These figures are of no material significance.

According to the criteria of hypertension as stated above, the incidence was 3.4 per cent in the entire group. The incidence in rheumatic children was 8 per cent, which is of interest in view of the association of hypertension with rheumatic heart disease later in life. On the contrary, it is believed that the hypertension discovered in children is probably transient and due to psychic influences, which well may be more prominent in the rheumatic child.

Although the number of functional murmurs has been included in all the tables presented, there has been no correlation with any factors discussed in this survey. Even the age groupings (5 to 9 years; 10 to 14 years; 15 to 19 years) failed to show any concentration of such cases.

CONCLUSIONS

1. The school populations of three California communities with markedly different climates were surveyed for the incidence of heart disease, rheumatic fever, functional heart murmurs, and hypertension

by a single skilled physician, using a uniform technique and uniform criteria of diagnosis. One of these communities was previously surveyed by a second physician, who used approximately the same technique and criteria.

2. Rheumatic fever and rheumatic heart disease occur in the warm, dry climate of Redlands in a degree comparable to cities with mild, temperate climates, such as Cincinnati and San Francisco.

3. Susanville, a mountain community with average humidity and precipitation, but with wide extremes of average winter and summer temperatures, presented a high incidence of rheumatic fever and rheumatic heart disease, comparable to the incidence in the northeastern United States or Great Britain.

4. Eureka, with a uniformly cool climate and high precipitation, presented an unusually high incidence of rheumatic disease, especially of valvulitis.

5. Congenital heart lesions were found in greater frequency than in all previous surveys except those reported previously from other California communities.

6. Children with rheumatic valvulitis gave fewer past histories and family histories of rheumatic fever than in other reports.

7. Certain statistical relations seem to exist between rheumatic disease and age, sex, race, and housing. Questionable relations exist to diet and to a history of scarlet fever. No definite relation of functional murmurs to any physical, symptomatic, or environmental influences, such as age, shape of chest, or nutritional state, was found.

REFERENCES

1. Halsey, R. H.: Heart Disease in Children of School Age, J. A. M. A. 77: 672, 1921.
2. Robey, W. H.: A Cardiac Survey of Children in Boston Public Schools, Nation's Health 9: 21, 1927.
3. Cohn, A. E.: Heart Disease From the Point of View of Public Health, AM. HEART J. 2: 275, 1927.
4. Cohn, A. E.: Heart Disease From the Point of View of Public Health, AM. HEART J. 9: 283, 1934.
5. Benjamin, J. E.: Heart Disease Situation in Cincinnati, AM. HEART J. 2: 637, 1927.
6. Newman, G.: Acute Rheumatism in Children in Its Relation to Heart Disease; Ministry of Health Reports on Public Health and Medical Subjects, No. 44, London, 1927.
7. Bainton, J. H.: Heart Disease and School Life, Am. J. Pub. Health 18: 1252, 1928.
8. Clark, T.: Heart Disease a Public Health Problem, Pub. Health Rep. 44: 2463, 1929.
9. Cahan, J. M.: Incidence of Heart Disease in School Children, J. A. M. A. 92: 1576, 1929.
10. Paul, J. R.: The Epidemiology of Rheumatic Fever, New York, 1930, Metropolitan Life Ins. Co. Press.
11. Paul, J. R.: The Epidemiology of Rheumatic Fever, New York, 1943, Metropolitan Life Ins. Co. Press.
12. Collins, S. D.: The Health of the School Child, Pub. Health Bull. No. 200, Washington, 1931, U. S. Treasury Dept.
13. Hewitt, E. S., and Geddie, K. B.: Report of Physical Examination of High School Students, Proc. Staff Meet., Mayo Clin. 6: 53, 1931.
14. Savage, W. G.: Incidence of Rheumatic Heart Disease in Childhood in Glouchestershire, Somerset and Wilts, Suppl., Brit. M. J. 2: 154, 1931.

15. Paul, J. R., Harrison, E. R., Salinger, R., and De Forest, G. K.: The Social Incidence of Rheumatic Heart Disease; A Statistical Study in New Haven School Children, Am. J. M. Sc. **188:** 301, 1934.
16. Cahan, J. M.: Rheumatic Heart Disease in Philadelphia School Children, Ann. Int. Med. **10:** 1752, 1937.
17. Sampson, J. J., Christie, A., and Geiger, J. C.: Incidence and Type of Heart Disease in San Francisco School Children, AM. HEART J. **15:** 661, 1938.
18. Bilderbeck, J. B., and Overstreet, R. M.: Incidence of Rheumatic Infections in Children in Oregon, Northwest. Med. **37:** 390, 1938.
19. Rauh, L. W.: Incidence of Organic Heart Disease in School Children, AM. HEART J. **18:** 706, 1939.
20. Paul, J. R.: Rheumatic Fever in New Haven, New York, 1941, Milbank Memorial Fund.
21. Hirsch, A.: Handbuch der Historisch-Geographischen Pathologie; Erlangen, 1860, Ferdinand Enke.
22. McClean, C. C.: The Age Incidence and Climatic Variations in Manifestations of So-Called Rheumatic Fever in White Children, J. Pediat. **2:** 320, 1933.
23. Seegal, D., Seegal, B. C., and Jost, E. L.: Comparative Study of Geographic Distribution of Rheumatic Fever, Scarlet Fever, and Acute Glomerulonephritis in North America, Am. J. M. Sc. **190:** 383, 1935.
24. Viko, L. E.: Heart Disease in the Rocky Mountain Region, AM. HEART J. **6:** 264, 1930.
25. Schwab, E. H., and Schulze, V. E.: The Incidence of Heart Disease and of the Etiological Types in a Southern Dispensary, AM. HEART J. **7:** 223, 1931.
26. Wood, J. E., Jones, T. D., and Kimbrough, R. D.: The Etiology of Heart Disease; Clinical Study of 623 Cases With Certain Observations on Race and Climate, Am. J. M. Sc. **172:** 185, 1926.
27. Fernando, P. G.: Rheumatic Heart Disease as Met With in Hospital Practice in Ceylon, Quart, J. Med. n.s. **8:** 261, 1939.
28. Cooper, E. L.: A Note on the Incidence of Rheumatic Infections in Australia, M. J. Australia **1:** 714, 1935.
29. Faber, Harold K.: A Weight Range Table for Children From 5 to 15 Years of Age, Am. J. Dis. Child. **38:** 758, 1929.
30. Faber, Harold K., and James, Charles A.: Range and Distribution of Blood Pressure in Normal Children, Am. J. Dis. Child. **22:** 7, 1921.
31. Taussig, H. B., and Hecht, M. S.: Studies Concerning Hypertension in Childhood; Occurrence of Hypertension in Acute Rheumatic Fever in Childhood, Bull. Johns Hopkins Hosp. **62:** 491, 1938.
32. Wilson, M. G., and Schweitzer, H. D.: Rheumatic Fever as a Familial Disease, J. Clin. Investigation **16:** 555, 1937. Additional data in Wilson, M. G.: Rheumatic Fever, New York, 1940, The Commonwealth Fund; London, 1940, Oxford University Press.
33. St. Lawrence, W.: The Family Association of Cardiac Disease, Acute Rheumatic Fever, and Chorea, J. A. M. A. **79:** 2051, 1922.
34. Paul, J. R., and Dixon, G. L.: Climate and Rheumatic Heart Disease, J. A. M. A. **108:** 2096, 1937.
35. Paul, J. R., and Salinger, R.: The Spread of Rheumatic Fever Through Families, J. Clin. Investigation **10:** 33, 1931.
36. Perry, C. B., and Roberts, J. A. F.: Study on the Variability in the Incidence of Rheumatic Heart Disease Within the City of Bristol, Suppl., Brit. M. J. **2:** 154, 1937.
37. McSweeney, C. J.: Acute Rheumatism in Childhood, Lancet **1:** 959, 1928.
38. Hedley, O. F.: Rheumatic Heart Disease in Philadelphia Hospitals. V. Distribution by Locality of Rheumatic Conditions in Philadelphia, Pub. Health Rep. **55:** 1854, 1940.
39. Rinehart, J. F., and Mettier, S. R.: The Heart Valves and Muscle in Experimental Scurvy With Superimposed Infection, With Notes on the Similarity of the Lesions to Those of Rheumatic Fever, Am. J. Path. **10:** 61, 1934.
40. Rinehart, J. F., Greenberg, L. D., and Christie, A. U.: Reduced Ascorbic Acid Content of Blood Plasma in Rheumatic Fever, Proc. Soc. Exper. Biol. and Med. **35:** 350, 1936.
41. Stimson, A. M., Hedley, O. F., and Rose, E.: Notes on Experimental Rheumatic Fever, Pub. Health Rep. **49:** 361, 1935.
42. Sendroy, J., and Schultz, M. P.: Studies of Ascorbic Acid and Rheumatic Fever. Part I. J. Clin. Investigation **15:** 369, 1937.
43. Perry, C. B.: Rheumatic Heart Disease and Vitamin C, Lancet **2:** 426, 1935.

CORONARY OCCLUSION AFTER FEVER THERAPY FOR SULFONAMIDE-RESISTANT GONORRHEAL URETHRITIS

MAJOR ABNER M. HARVEY, M.C., ARMY OF THE UNITED STATES, AND
MAJOR FREDERICK T. BILLINGS, M.C., ARMY OF THE UNITED STATES

FEVER therapy has been used in the treatment of eighty-five patients in a General Hospital. The electrocardiograms of three of these patients showed progressive changes typical of coronary occlusion of the anterior type. The patients were young adult males who had no disease other than chronic gonococcal urethritis which was resistant to sulfonamide therapy. Coronary occlusion as a complication of fever therapy has been observed rarely,[1] and the effects of such an occurence on persons of this age who were previously in excellent health is of considerable interest.

Fever therapy has been used in this hospital to treat neurosyphilis and nonspecific iridocyclitis, but for the most part in treating sulfonamide-resistant gonorrhea. A full course of therapy consisted of maintaining a rectal temperature at 106 to 107° F. for five to seven hours. Gonorrhea was considered resistant to sulfonamide therapy after the administration of 35 Gm. of sulfathiazole in five days, followed for five more days by the same amount of sulfadiazine. This was in addition to sulfonamide therapy which was given in many cases prior to the admission of the patient to this hospital.

Prior to the fever therapy the sulfonamide was discontinued for a period of one week. On the day before the hyperpyrexia, 10 Gm. of sodium chloride and 3,000 c.c. of water were given by mouth between noon and bedtime. The patient was encouraged to take a full diet, with 10 Gm. of brewer's yeast in addition. At bedtime 3 Gm. of sulfathiazole were administered by mouth, and in the morning an additional 2 Gm. were given. Just before entry into the cabinet, 15 c.c. of paraldehyde were given orally, and further sedation during the course of the treatment consisted of 8 mg. of morphine in the first hour, followed several hours later by 0.3 mg. of scopolamine. For the most part the patients were quiet and cooperative during the treatment. The average time taken for the rectal temperature to reach 106° F. was one and a half hours. As the temperature varied between 106 and 107,° the pulse rate ranged from 140 to 160 per minute. Iced physiologic saline was given by mouth throughout the treatment, and the average intake was 1,500 to 2,000 cubic centimeters. The temperature elevation was maintained by means of radiant heat supplied by ten 100-watt electric light bulbs in an atmosphere approaching

Received for publication April 26, 1944.

100 per cent humidity. The temperature of the patient could be controlled easily by varying the intensity of the heat and by applying ice water to the head. On removal from the cabinet the blood pressure was taken and varied from 70/50 to 120/75. On return to the ward after the temperature had become normal, 1,000 c.c. of 5 per cent glucose in normal saline solution were given intravenously. The patient remained in bed thirty-six hours. In the cases of coronary occlusion this routine was followed, and the patients completed the full course of fever with no difficulty or unusual discomfort.

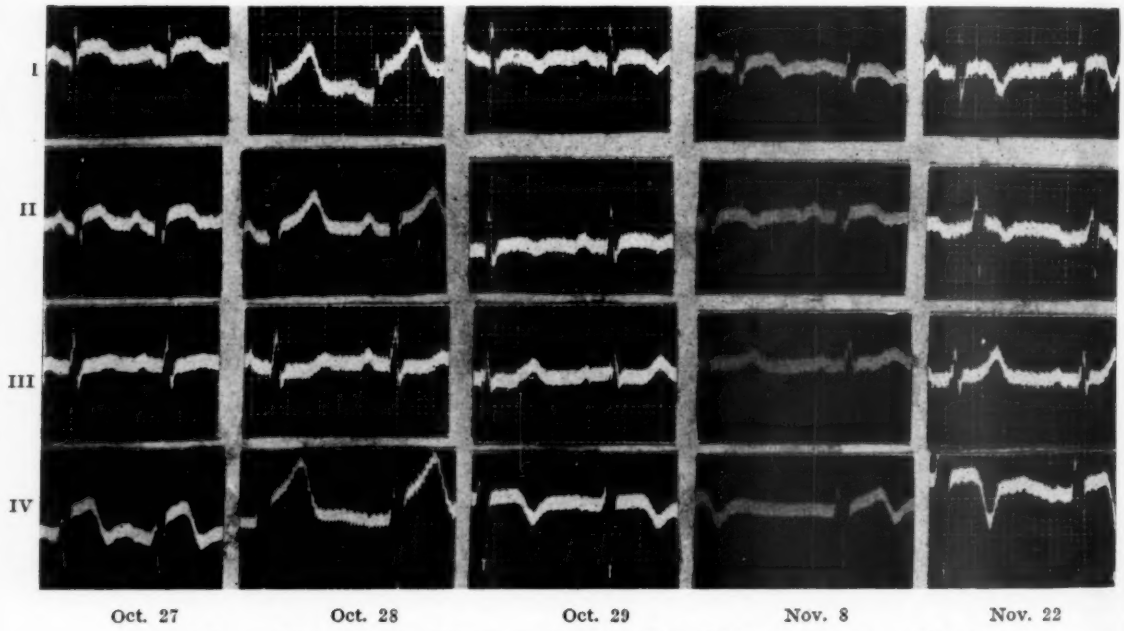


Fig. 1.—Case 1. Fever therapy on Oct. 26, 1943. October 27: Lead I. The QRS complex is of low amplitude. The S-T segment is slightly elevated, and ends in a biphasic T wave. Lead II. The appearance of the S-T segment and T wave is similar in this lead. Lead III: The T wave is upright. Lead IV: There is almost complete absence of the R wave. The S-T segment is elevated and ends in a biphasic T wave. October 28: The S-T segments in Leads I, II, and IV are elevated. The T waves in these leads are large and upright. The S-T segment in Lead III is slightly depressed, and the T wave is biphasic. October 29: The T waves are now definitely inverted in Leads I, II, and IV. November 8: The S-T segments are still arched; the T waves are inverted in Leads I and II, and biphasic in Lead IV. November 22: The T waves are now deeply inverted in Leads I, II, and IV.

Impression.—The progressive changes in these records are typical of those which occur after occlusion of the anterior descending branch of the left coronary artery. In this case the T waves were still abnormal ten weeks after the onset of the illness.

CASE REPORTS

CASE 1.—This 24-year-old patient had gonococcal urethritis for which he was treated for four weeks prior to admission to this hospital with sulfathiazole and sulfadiazine. He received routine sulfonamide therapy here, with no improvement in his gonorrhea. Physical examination showed a normal cardiovascular system, with a blood pressure of 120/65. A roentgenogram of the heart was normal, but no electrocardiogram was taken prior to fever therapy. During the treatment

his pulse was regular and of good quality, and at no time did the rate exceed 160 beats per minute. During the period in the cabinet he took 2,400 c.c. of physiologic saline by mouth, and was quiet and cooperative. On removal from the cabinet his blood pressure was 70/50. When his temperature returned to normal his pulse rate was 86, and, after the intravenous treatment, his blood pressure rose to 100/60.

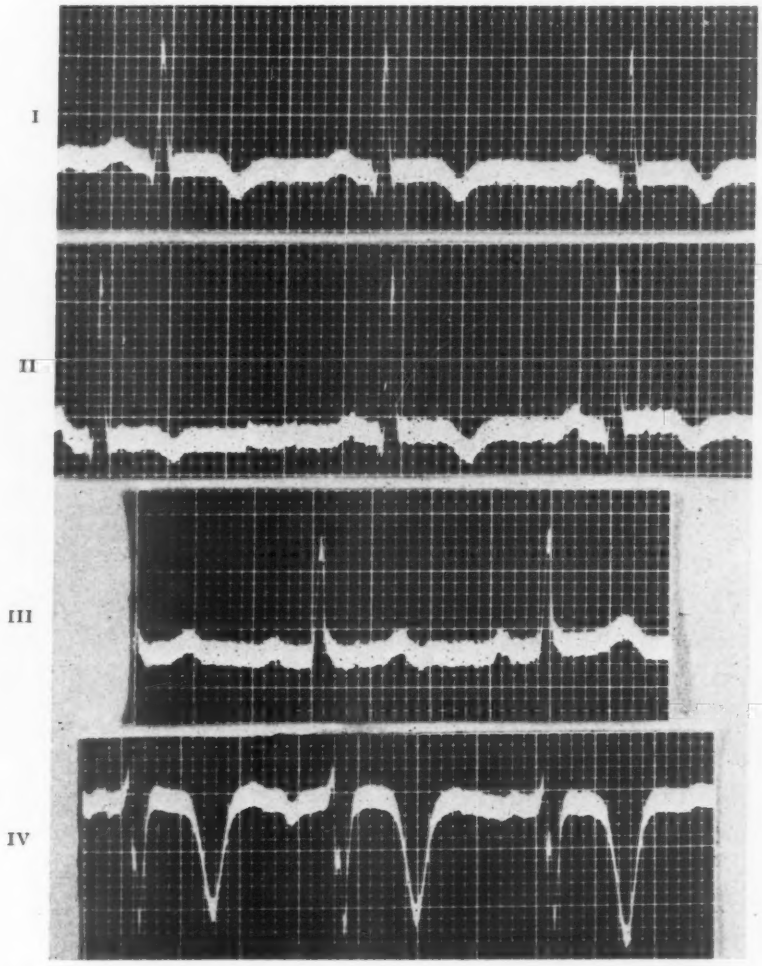


Fig. 2.—Case 2. Fever therapy on Nov. 19, 1943. December 23: Lead I: The S-T segment is arched, and ends in an inverted T wave. Lead II: The S-T segment has the same appearance as in Lead I, but the T wave is not so deeply inverted. Lead III: essentially normal in appearance. Lead IV: An auricular premature beat is visible. The R wave is almost entirely absent, and the T wave is very deeply inverted.

Impression.—These changes are typical of those which occur with coronary occlusion of the anterior type. An electrocardiogram taken on March 5, 1944, showed normal T waves, but the R wave in Lead IV was still very small.

The following morning he complained of a moderately severe, oppressive feeling beneath the sternum. He appeared rather apprehensive and pale, but was quiet. His blood pressure was 70/40, and his pulse rate, 84. The heart sounds were distant. Four hours later his symptoms had

completely subsided and he felt quite normal. His blood pressure remained at 85/50. For two days after the treatment he had fever, with a temperature up to 102° F., and for one week there were a moderate leucocytosis and acceleration of the sedimentation rate to 30 mm. per hour. His blood pressure did not return to normal for ten days. The electrocardiographic changes are described in Fig. 1.

CASE 2.—Before admission to the hospital this 19-year-old patient had received "large doses" of sulfonamides for a fifteen-day period.

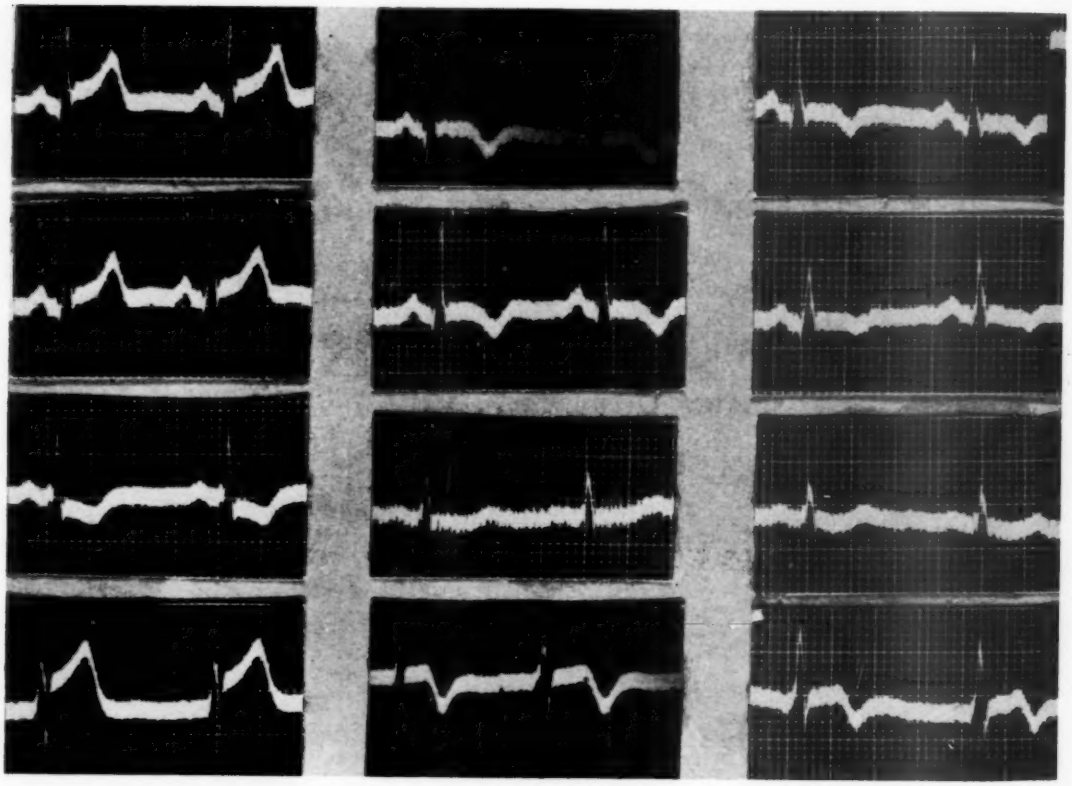


Fig. 3.—Case 3. Fever therapy on Nov. 30, 1943. December 1: There is elevation of the S-T take-off in Leads I and II, and to a greater extent in the chest lead. Slight depression of this segment in Lead III, ending in a biphasic T wave. The QRS complex in Lead IV is of low amplitude, and the R wave is a little slurred. December 3: In this record the T wave is deeply inverted in Leads I, II, and III. The QRS complex is still very small in Lead IV, and the R wave is slurred. December 16: There is still inversion of $T_{1, 2 \text{ and } 4}$. T_3 has a tendency to be biphasic. The R wave in Lead IV is now much larger.

Impression.—The progressive changes in these records are indicative of coronary occlusion, probably anterior in type. A record taken Jan. 30, 1944, still showed inversion of T_4, but the other T waves were upright.

Prior to the fever treatment he received 35 Gm. of sulfathiazole in five days, followed during the next five-day period by 35 Gm. of sulfadiazine. There was no lessening of the urethral discharge, and no toxic manifestations of the drug therapy were noted. This patient was given the routine preparation for fever therapy. On physical examination his heart and lungs were normal, and his blood pressure was 115/75.

During fever therapy, his temperature rose from normal to 106° F. in eighty-eight minutes. His pulse was regular and of good quality throughout the treatment, with a rate between 140 and 160 per minute. The fluid intake during his stay in the cabinet was 1,800 c.c. of physiologic saline orally. One hundred fifty minutes after removal from the cabinet his blood pressure was 110/50, and his pulse rate was 116 per minute. The pulse rate soon fell to 86 per minute. The following day he felt normal, and was soon discharged from the hospital, cured of his urethral discharge. Five weeks later he was readmitted to another hospital for a second gonorrheal infection, and an electrocardiogram was made preparatory to further fever therapy. Although the patient felt perfectly well, and although physical examination was negative and his blood pressure was perfectly normal, the electrocardiogram showed the typical T-wave changes which follow occlusion of the anterior descending branch of the left coronary artery (Fig. 2).

CASE 3.—This 25-year-old patient was admitted to the hospital because of gonococcal urethritis. He received sulfathiazale and sulfadiazine according to the usual routine, with no improvement. This was followed one week later by fever therapy, with a temperature of about 105.6° F. for eight hours. He took 1,500 c.c. of physiologic saline by mouth; his pulse rate remained below 160 per minute, and he did not become restless or have any complaints. The next morning, about sixteen hours after removal from the cabinet, he complained of a numb feeling in both arms and a sensation of tightness and aching pain beneath the upper part of the sternum. He was fairly apprehensive, but his breathing was quiet and he was not cyanotic or dyspneic. The lungs were normal. The heart was not enlarged, the sounds were of quite good quality, and no murmurs were audible. The blood pressure, which had been 120/60 before treatment, was now 106/70. He appeared well hydrated, and the hematocrit reading was normal. An electrocardiogram taken at this time showed changes typical of coronary occlusion of the anterior type (Fig. 3). There was a slight rise in temperature, the leucocyte count rose to 13,000 per c. mm., and the sedimentation rate was 14 mm. per hour. Two days later he still complained of pain, and at that time had tenderness in the region of the left trapezius muscle. The blood pressure had risen to normal, and examination of the heart revealed no abnormalities. At no time was he acutely ill. His urethral discharge disappeared after the fever therapy and did not return. Recovery was uneventful. The electrocardiogram showed the progressive changes characteristic of occlusion of the anterior descending branch of the left coronary artery. Residual changes were still present in records made eight weeks after the onset of the illness.

DISCUSSION

Three patients developed electrocardiographic changes typical of occlusion of a coronary artery after fever therapy for sulfonamide-resistant gonococcal urethritis. All of these patients were healthy young soldiers; their ages were 24, 19, and 25 years, respectively. In none of these cases was there any reason to suspect any abnormality of the cardiovascular system prior to the treatment. In one case there were never any symptoms referable to the heart, and in the other two they were relatively mild and the patients were never seriously ill.

These facts, coupled with the drastic nature of the therapy, make it reasonable to assume that this complication is more widespread than has been previously suspected, and that electrocardiograms should be taken routinely before and during the twenty-four- to seventy-two-hour period after fever therapy. The development of this type of cardiac lesion as an aftermath of fever treatment has been reported but rarely. In the three cases described here, the progressive changes in the electrocardiogram were typical of occlusion of a coronary artery, and they persisted for the entire time the patients were under observation, which varied from six to ten weeks.

Trautman[2] has reported the complications in a series of 6,881 treatments with therapeutic hyperpyrexia. The blood pressure fell to 80 mm. Hg, systolic, or below, in 8.5 per cent of the patients. It seems possible that, among this group, cases of the type described in this communication might have been discovered if electrocardiograms had been taken.

After these cases were observed, records were made routinely before and for three days after therapeutic hyperpyrexia in a series of fifteen cases. In two cases, other than those reported, the electrocardiograms showed a coronary type of S-T segment and T-wave change within twenty-four hours which persisted for several days, but then reverted to normal. Neither patient had any complaints referable to the cardiovascular system. In several others, a transient cardiac arrhythmia was observed in additon to minor changes in the S-T segments and T waves; this was of short duration (Fig. 4).

In view of the typical electrocardiographic abnormalities in these three cases, with progressive changes persisting after five to ten weeks, the diagnosis of coronary occlusion seems quite conclusive. The pathogenesis of the occlusion is not clear. Miller and Woods[3] analyzed twelve cases of coronary thrombosis occurring in patients between the ages of 20 and 30 years. Ten of their patients were men and two were women. There was no predilection for race or occupation. Four died in the first attack. There was a history of rheumatic fever in one, and in none was syphilis the cause. Atheroma or atherosclerosis was found in all four cases in which there were adequate autopsy data. The anterior descending branch of the left coronary artery was most frequently the site of thrombosis.

It is possible that in the cases of the present series an atheromatous nidus existed, and that changes in fluid and electrolyte balance or in the coagulability of the blood as a result of the prolonged high temperature might have been the precipitating factor. It is of interest, in view of the autopsy observations noted above, that in all of these cases the electrocardiograms pointed to the anterior descending branch of the left coronary artery as the seat of the thrombosis. The patients in the present series recovered promptly from their symptoms, but continued

to have abnormal electrocardiograms for many weeks after the onset, so that the effect on the state of the cardiovascular system in the future cannot be predicted. The serious nature of this complication makes it desirable to take electrocardiograms routinely before and during the twenty-four- to seventy-two-hour period after fever treatment. Only in this manner can those cases in which there are few or no symptoms

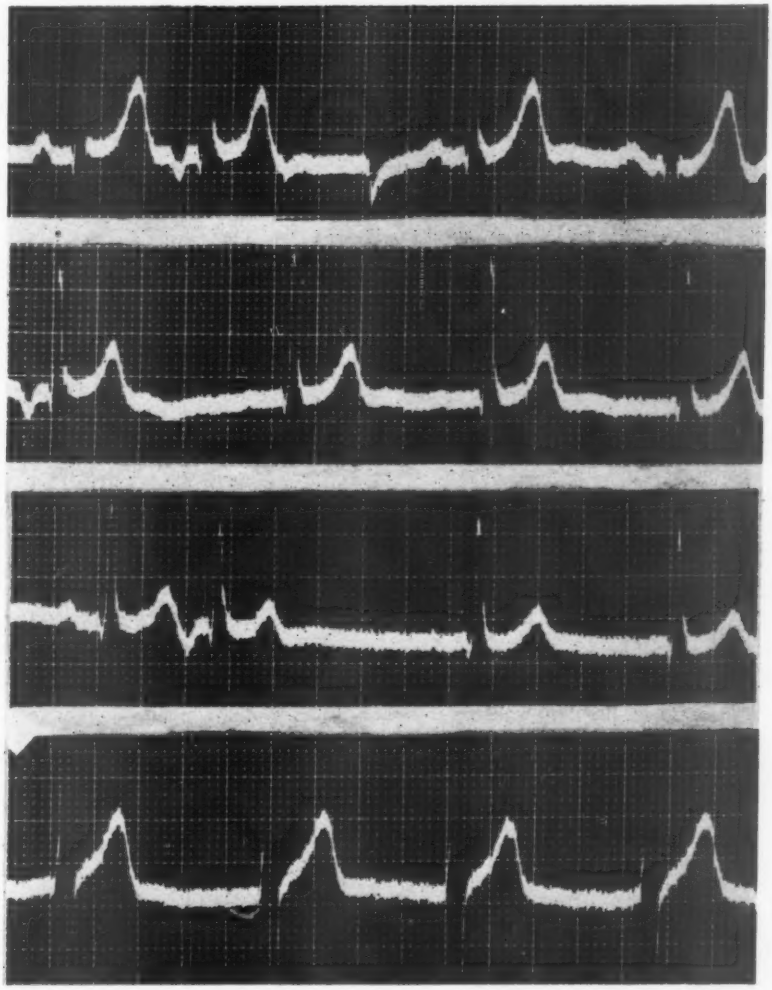


Fig. 4.—This record, taken forty-eight hours after fever therapy, shows one type of cardiac arrhythmia which may occur. There were numerous auricular premature beats, some of which were followed by short periods of A-V nodal rhythm. This persisted for four days after termination of the therapeutic hyperpyrexia. Leads I to IV, from above downward.

be recognized and proper therapy instituted. It is of interest that one patient in this series never had any cardiac symptoms, was discharged without any restriction of activity, and five weeks later had a routine electrocardiogram which revealed the diagnosis. In view of the appar-

ent frequency and the possible effect on the future health of the patient of this complication, it is recommended that penicillin be used in the treatment of sulfonamide-resistant gonococcal infections whenever it is possible.

SUMMARY

1. Three cases of coronary occlusion occurred after the administration of therapeutic hyperpyrexia for sulfonamide-resistant gonococcal urethritis.

2. All of the patients were young adult males and had no preexisting disease of the cardiovascular system. In no instance was the patient critically ill.

3. Electrocardiograms in each case showed progressive changes similar to those which occur with occlusion of the anterior descending branch of the left coronary artery. In two cases, definite T-wave changes were still present eight and ten weeks after the onset. In the third, a record made fifteen weeks after the therapeutic hyperpyrexia revealed normal T waves.

REFERENCES

1. Dawber, T. R.: Coronary Occlusion Following Fever Therapy, Virginia M. Monthly 68: 156, 1941.
2. Trautman, J. A.: Artificial Fever Therapy: Its Management and a Report of Complications of 6,881 Treatments, Arch. Phys. Therapy 23: 197, 1942.
3. Miller, W. S., and Woods, W. W.: Fatal Coronary Thrombosis in a Man Aged Twenty-two; Brit. Heart J. 5: 2, 101, 1943.

PERIODIC CHANGES IN THE FORM OF THE P WAVES IN PARTIAL HEART BLOCK

DAVID SCHERF, M.D.
NEW YORK, N. Y.

IN EXPERIMENTAL[1] and clinical heart block[2, 3] a peculiar disturbance of the auricular rhythm may be observed; it consists of a prolongation of one or two of the auricular cycles which follow ventricular contractions. This phenomenon was attributed to rhythmic variation of vagal tonus.[1] Reflex inhibition of the heart by stimulation of the pressor nerves in the aorta and carotid sinus can wax and wane within one single cycle.[4, 5, 6] These periodic changes in auricular rate are not rare.

The phenomenon was markedly developed in nine out of fifteen cases of complete heart block; in three other cases in the same series it was inconstant and less distinct, but in only three patients was it absent.[7] It is very common in 2:1 block. Here the auricular periods during which a ventricular contraction occurs are shorter than the others, and the P waves which follow a ventricular contraction seem premature. The differentiation from auricular extrasystoles is therefore necessary and usually easy. The form of the P waves remains constant in cases of heart block, whereas the premature P wave in auricular extrasystoles usually shows a different form.

Auricular extrasystoles which originate in the sinus node have P waves of the same form as those of the sinus beats; accordingly, the picture is similar to 2:1 block with alternating length of the auricular period, but such extrasystoles are very rare. In most cases of partial heart block exercise produces a change in the type of the block, and this would aid in differential diagnosis.

In heart block, however, periodic changes in the form of the P waves may occur; they are independent of the disturbance of rate, but sometimes they are combined with it.

The electrocardiogram shown in Fig. 1 was obtained from an 18-year-old patient with rheumatic fever. The P waves are abnormally wide and split, and there is left axis deviation with some slurring of the QRS complexes. The tracings show 2:1 block, with delayed auriculoventricular conduction interchanging with periodically dropped beats. The patient had not received digitalis. It is clear that those P waves which appear after a long ventricular diastole have a different form than those which appear soon after a T wave. The change is present in all leads and is most marked in Lead II. In this tracing the P waves

From the Department of Medicine, New York Medical College.
Received for publication April 26, 1944.

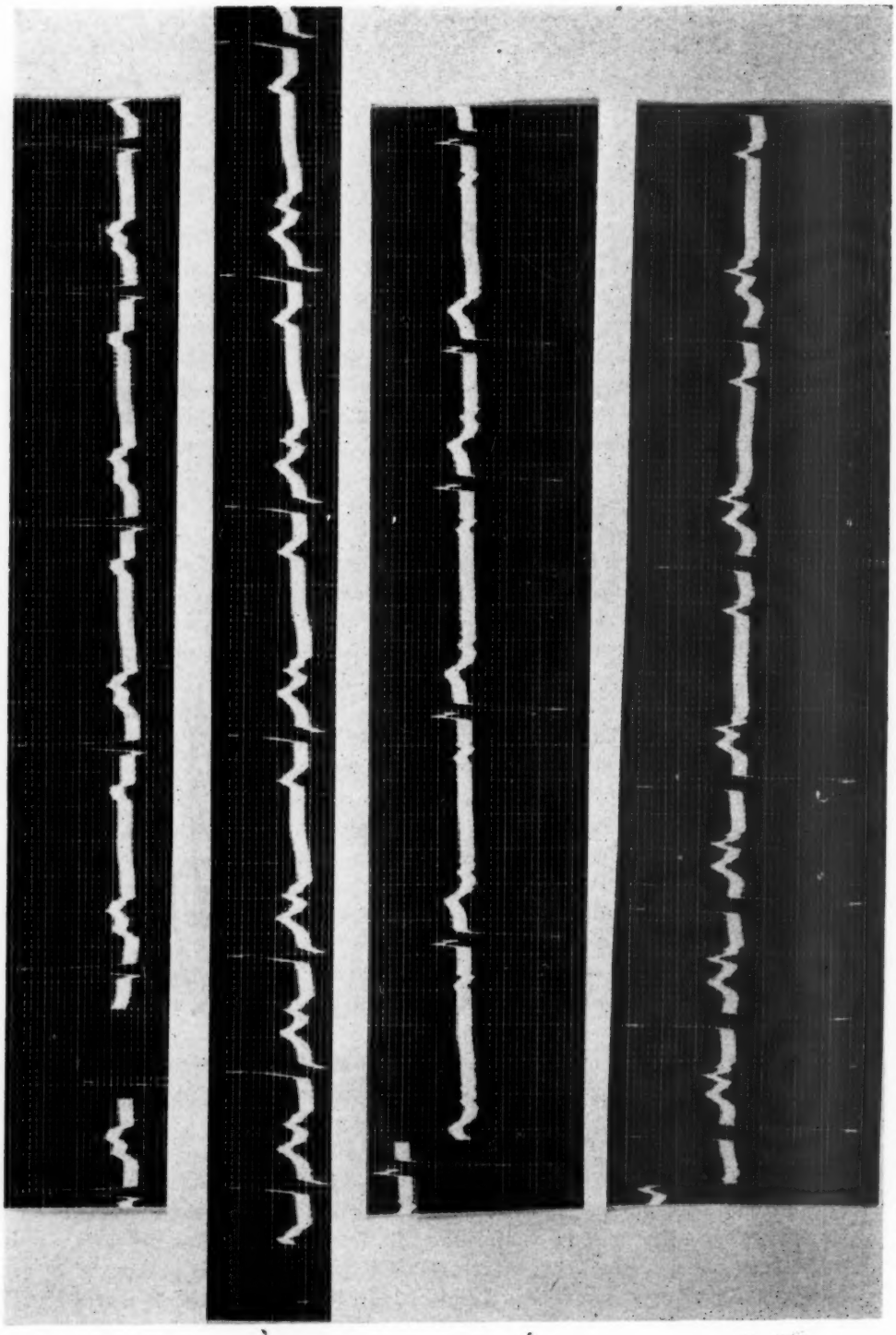


Fig. 1.—Leads I, II, III, and CR_4; 2:1 block and periodically dropped beats, with periodic changes in the form of P waves.

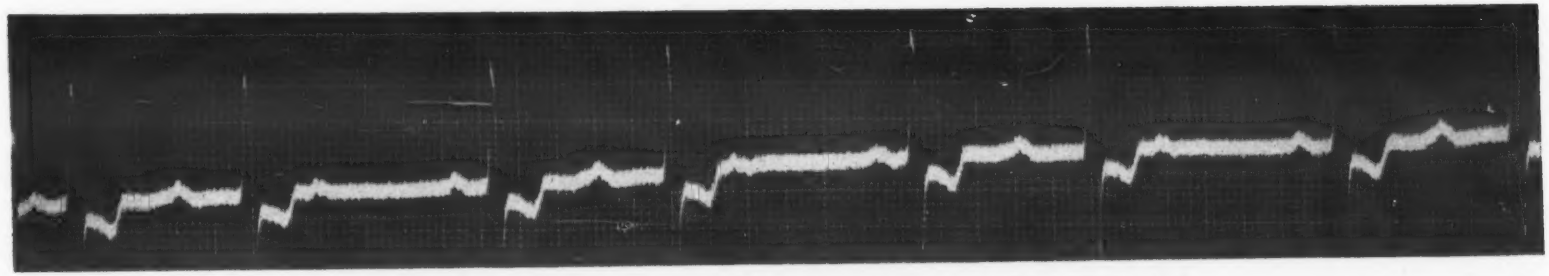


Fig. 2.—Periodically dropped beats with changes in the form of the P waves (CR_4).

which appear after a longer ventricular diastole are sharper and do not show notching in the downstroke, as do the other P waves. During the series of conducted beats the form of the P waves is constant. The change, however, is always present during the 2:1 block.

The auricular cycle which includes a ventricular contraction measures 0.64 second, whereas the others measure 0.68 to 0.70 second. The P waves of abnormal configuration appear, therefore, to be slightly premature.

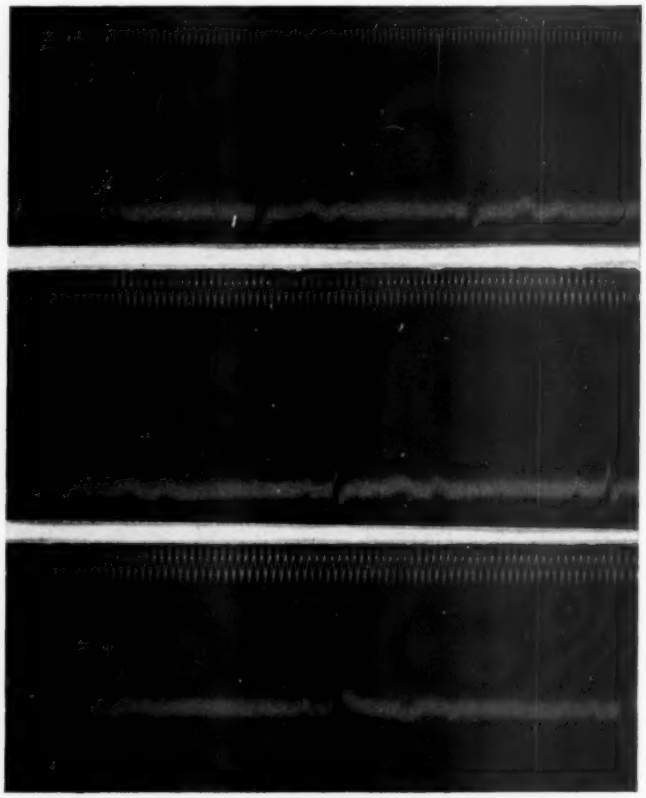


Fig. 3.—Changes in the P waves and 2:1 block.

Fig. 2 was obtained from a 48-year-old patient with rheumatic aortic insufficiency during a recurrence of his rheumatic fever (Lead CR_4). The patient had not received digitalis. The electrocardiogram shows periodically dropped beats (Wenckebach's periods). In this tracing, again, those P waves which follow a ventricular complex rather closely have a different form than the others. They are low and more split. The auricular rate is regular.

Fig. 3 shows the three limb leads of an electrocardiogram obtained from a 65-year-old patient with coronary sclerosis and angina pectoris. There is a 2:1 block, and a deep Q wave is visible in Lead III. In

Lead I the blocked P wave, coming early in diastole, is higher than the conducted P wave. In Lead III the blocked P wave is inverted, whereas the conducted P wave is positive. Prolonged observation of this patient and exercise tests proved that we were dealing with 2:1 block, and not a bigeminal rhythm due to blocked auricular extrasystoles. The P-P interval which includes a ventricular complex measures 0.74 second; the following or the preceding one measures 0.80 second. The abnormal P wave is therefore premature.

Fig. 4 shows two tracings, obtained from two different patients with 2:1 block. The upper tracing was taken from a patient with coronary sclerosis, and the lower from a patient with rheumatic fever. Both tracings are Lead II. In the upper tracing the blocked P wave is

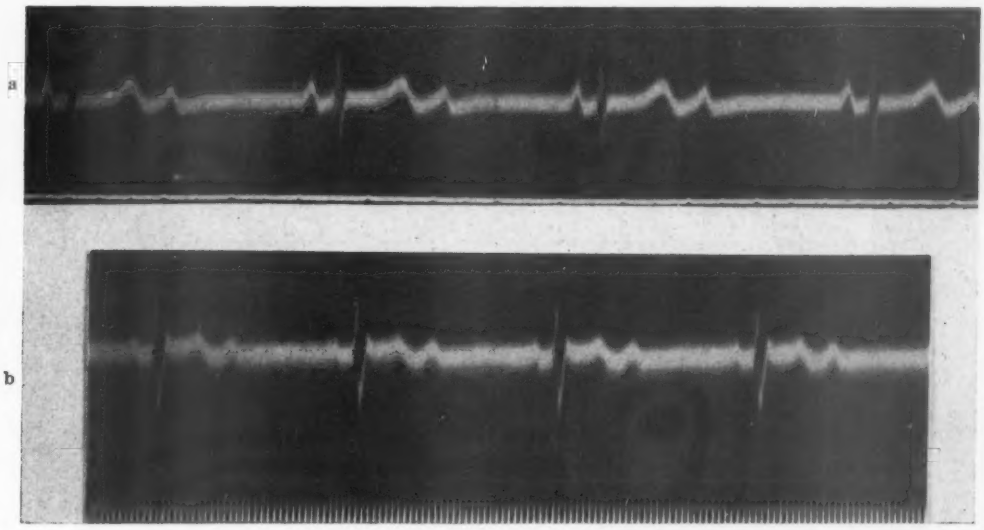


Fig. 4.—Two cases of 2:1 block with alternation in the form of the P waves.

lower, and in the lower tracing it is higher and broader, than the P wave which is conducted to the ventricle. A tracing obtained after an exercise test in the second case, which was published in another connection[8] elsewhere, shows that a conduction disturbance exists, and not extrasystoles. In the upper tracing the P-P intervals which include a ventricular complex measure 0.78, the others 0.84, second. In the bottom tracing the corresponding values are 0.59 and 0.68, respectively. In both cases, therefore, the length of the auricular cycle alternates, and the cycle during which the ventricle contracts is shorter.

DISCUSSION

In all five cases partial heart block existed, and in all cases only those P waves were abnormal which appeared early after a QRS complex.

Changes in the form of the P waves in partial or complete heart block are known to occur. The disturbance, however, is always visible for a series of beats, and does not concern exclusively those P waves which come early after a QRS complex. It is independent of ventricular activity, and is due to the fact that the disease which causes the heart block (diphtheria, coronary sclerosis) also involves the auricles and causes a shift of the pacemaker or a disturbance of intra-auricular conduction. The changes in the form of the P waves mentioned in this paper have not—as far as we can ascertain—been described before.

In those cases in which the alternation in the form of the P waves is combined with an alternation in the length of the auricular periods, confusion with auricular extrasystoles is easily possible. In all five cases, analysis of long tracings or exercise tests permitted one to exclude the presence of auricular extrasystoles.

In the first two cases (Figs. 1 and 2) the disturbance persisted as long as the partial heart block lasted, that is, for two and four days, respectively. In the other three cases no follow-up study was possible.

An explanation of this disturbance which comes to mind first is that there is superimposition of a U wave on those P waves which appear early in diastole and follow the T waves at an appropriate distance. It is known that, under some conditions, for instance in tachycardias, this summation may alter the form of the P waves, and this mechanism may play a role in some of the tracings reported. A study of other tracings, however, like that of Fig. 2, shows that the periodic alteration of the form of the P waves appears independent of U waves; the first, third, and fifth QRS complexes of this tracing show this clearly. The T waves of these QRS complexes are not followed by a U wave. Therefore, those abnormal P waves which appear a short distance after the T wave are not altered by summation with a U wave. Although U waves may be inverted, they are not sharp and peaked like the waves following the T waves in Lead III of Fig. 3.

Sometimes abnormal and premature P waves follow the QRS complex at a short interval in complete heart block. Originally they were explained as a result of mechanical irritation of abnormal auricular centers by the ventricular systole; the latter was supposed to induce the formation of a heterotopic stimulus. These premature, abnormal P waves are now explained better by a retrograde conduction of ventricular automatic beats to the auricle. This mechanism can easily be ruled out for the cases described in the present paper.

It is more probable that the same mechanism which causes the auricular rate to change, that is, variation of the vagal tonus in heart block, also influences the site of formation of stimuli or their spread over the auricle, and is in this way responsible for the abnormal form of the P waves in partial heart block.

SUMMARY

Five cases of partial auriculoventricular block are reported, in which those P waves which came early in diastole constantly had an altered shape. In four of these cases, during 2:1 block, the P waves with an abnormal configuration seemed to be slightly premature.

Knowledge of this disturbance will prevent confusion with blocked auricular extrasystoles.

Sometimes this change of form may be due to superimposition of U waves on early P waves. Another possibility is a change in intra-auricular conduction or site of stimulus formation caused by varying vagal tone.

REFERENCES

1. Erlanger, J., and Blackman, J. R.: Further Studies in the Physiology of the Heart Block in Mammals, Heart **1**: 177, 1909.
2. Hecht, A.: Der Mechanismus der Herzaktion im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **11**: 324, 1913.
3. Wilson, F. N., and Robinson, G. C.: Heart Block, Arch. Int. Med. **21**: 166, 1918.
4. Ashman, R., and Gouaux, J. L.: Reflex Inhibition of the Human Heart: Complete A-V Block and Parasystole, Proc. Soc. Exper. Biol. & Med. **37**: 25, 1937.
5. Brown, G. L., and Eccles, J. C.: The Action of a Single Vagal Volley on the Rhythm of the Heart Beat, J. Physiol. **82**: 211, 1934.
6. Brown, G. L., and Eccles, J. C.: Further Experimentation on Vagal Inhibition of the Heart Beat, J. Physiol. **82**: 242, 1934.
7. Kauf, E.: Über Rhythmusschwankungen des Vorhofes bei Herzblock, Zentralbl. f. Herz-u. Gefässkr. **18**: 85, 1926.
8. Scherf, D.: Über intraventrikuläre Störungen der Erregungsausbreitung bei den Wenckebachschen Perioden, Wien. Arch. f. inn. Med. **18**: 403, 1929.

NEGATIVE DISPLACEMENT OF THE RS-T SEGMENT IN THE ELECTROCARDIOGRAM AND ITS RELATIONSHIPS TO POSITIVE DISPLACEMENT; AN EXPERIMENTAL STUDY

CHARLES C. WOLFERTH, M.D., SAMUEL BELLET, M.D.,
MARY M. LIVEZEY, M.D., AND FRANKLIN D. MURPHY, M.D.
PHILADELPHIA, PA.

NEGATIVE displacement of the RS-T segment of the electrocardiogram is common. Study of the literature relating to the mechanisms concerned in its development is, however, not highly illuminating, chiefly, we believe, for two reasons. In the first place, remarkably little experimental work has been done in the attempt to explain it. Second, the relationships of negative displacement in body surface electrocardiograms to potential changes at cardiac surfaces during that interval are not well enough understood.*

Recent studies have indicated that, in general, potential variations of ventricular origin on the surface of the right arm are relatively smaller in magnitude than those of the left arm and left leg,[1-3] and that, in Leads I and II, the patterns of differences of potential usually bear some resemblance to the patterns of potential variation of the left arm and left leg, respectively. Thus, the probability is that, in concordant negative displacement, potential of cardiac origin distributed to both the left arm and left leg is negative during that interval, and that negative potential change is also present over at least part of the epicardial surface of the anterolateral wall of the left ventricle and part of the posterior surface in close contact with the diaphragm. It is therefore possible that the negative displacement recorded in limb leads by Scherf and Boyd[4] after trauma to the inside of the left ventricle reflected negative potential change at posterior and anterolateral surfaces of the left ventricle. Our observations on negative RS-T segment displacement, both experimentally and in acute myocardial infarction, have led us to believe that its direction in Lead II reflects the same direction of potential change on the posterior surface of the left ventricle. Some evidence for that correlation will be furnished in this study.

From the Edward B. Robinette Foundation, Medical Clinic, Hospital of the University of Pennsylvania, and the Division of Cardiology of the Philadelphia General Hospital.

Read in abstract, April 20, 1944, at the Inaugural Program of the Instituto Nacional de Cardiologia, Mexico, D. F.

Received for publication May 29, 1944.

*We make the conventional assumption that, when one electrode is placed in contact with a cardiac surface, and the other placed at a distance from the heart, the recurrent patterns of differences of potential corresponding to ventricular activity represent potential fluctuations or variations transmitted to the electrode in contact with the heart, and that, consequently, such electrocardiograms reflect a continuous record of the mean potential variations of the surface area in contact with the electrode.

In dealing with RS-T segment displacement in chest leads, one is on somewhat firmer ground than has been the case in limb leads, because correlation between the direction of RS-T potential change on the anterior and left anterolateral aspects of the epicardium and the overlying precordium has been more definitely established. Segment displacement in CR leads, or leads in which the exploring electrode is placed over a part of the precordium and paired with one placed over the spine of the right scapula, we believe, reflects with a high degree of accuracy the direction of potential change at the underlying epicardial surface.

HISTORICAL SUMMARY

Engelmann, in 1873, was the first to demonstrate "monophasic" curves resulting from cardiac injury, according to Burdon-Sanderson and Page[5] (Engelmann's article was not available to us), who confirmed the observation. Bayliss and Starling[6] state that Waller, who showed that "monophasic" curves can also be recorded from mammalian hearts, at first regarded them as a normal phenomenon, but later attributed them to injury. Bayliss and Starling, however, showed beyond question the relationship in the mammalian heart between cardiac injury and what would now be regarded as segment displacement.* These studies long antedate Samojloff's[7] demonstration, in the cold-blooded heart, of RS-T segment displacement after injury, by means of the Einthoven galvanometer. Eppinger and Rothberger[8] obtained evidence to indicate that the direction of RS-T segment displacement in recto-esophageal leads may depend on the part of the heart subjected to injury. The experimental data are open to some question, but the importance of the concept is not.

The awakening of interest in the electrocardiographic study of the effects of coronary obstruction on the myocardium followed Smith's[9] pioneer experimental work on that subject, in which limb leads were used. This was quickly followed by Pardee's[10] observations on electrocardiographic changes in human coronary obstruction. Parkinson and Bedford[11] and Barnes and Whitten[12] then established the limb lead criteria by which infarction involving the anterior and posterior walls of the left ventricle could be differentiated.

In the meantime, chest leads were almost forgotten, although they were used occasionally by Lewis and others to obtain information regarding abnormalities of auricular mechanism. Otto,[13] however, used them in 1929 for the specific purpose of studying experimentally the effects of myocardial injury. He demonstrated that, after injury to the dog's heart, RS-T segment displacement appeared in a lead made with both electrodes on the front of the chest.

In 1932, Wolferth and Wood[14] reported observations on chest leads in human anterior myocardial infarction. With the polarity used at that time, the RS-T segment was recorded as displaced downward. It would now be recognized as positive displacement. On the basis of experimental studies by Wood, Wolferth, and Livezey,[15] completed at the time of that publication but not published until 1933, it was predicted that, in human posterior infarction, the direction of the RS-T segment displacement in chest leads would be opposite to that of anterior infarc-

*In the same paper, Bayliss and Starling concluded that leading from the apex and the right arm yields the largest deflections and is, therefore, favorable.

tion, as had been found to be the case in dogs. This prediction was verified later in 1932[16] by the publication of chest leads obtained before and shortly after posterior infarction. In 1938, Wood, Wolferth, and Bellet[17] also showed that negative RS-T segment displacement in a lead with one electrode placed over or outside the apex is one of the characteristic changes in acute lateral infarction.

In the meantime, Wilson and his co-workers[18] had published their study of bundle branch block, which furnished evidence that patterns of precordial leads tended to resemble those obtained when the exploring electrode was placed on corresponding underlying epicardial surfaces. Another observation by Wilson et al.,[19] which is pertinent to our present subject, was that, in the turtle heart, negative RS-T segment displacement could be recorded at an epicardial area distant from the area of injury. Bellet and Johnston[20] confirmed Wood, Wolferth, and Livezey's observation that deprivation of blood supply to the posterior wall produces RS-T segment displacement on the anterior wall opposite in direction to that obtained over the area deprived of its blood supply.

In contrast to the meager experimental data bearing on the subject of negative RS-T segment displacement, there have been numerous clinical studies in which this phenomenon has been recorded. It is well known that, in addition to its presence in chest leads in acute posterior infarction, negative displacement over and above the slight negative displacement sometimes observed in normal subjects may be recorded both in Lead II and in chest leads following acute lateral infarction, during attacks of angina pectoris, as a digitalis or epinephrine effect, or as a result of other toxic states, and in the so-called hyperventilation syndrome.[21] It may be present constantly in association with hypertensive states, and in certain cases of left ventricular hypertrophy without hypertension. It is found occasionally during a state of shock, and may be produced by carbon monoxide poisoning (Bellet, unpublished observations) or in certain persons by reduction of the percentage of oxygen in the respired air. It has been shown to be present in certain cases of coronary insufficiency in which lesions were suspected, or at least deficiency of oxygen supply, involving the endocardial side of the heart wall.[22] Consequently, because of the clinical importance of negative displacement and the unsatisfactory status of our knowledge as to the modes of its production, an experimental study was undertaken. This study concerned itself with efforts to produce negative displacement in leads made with an exploring electrode on cardiac surfaces, and observations on its relationships to positive displacement.

REPORT OF EXPERIMENTS

Methods.—Dogs were anesthetized deeply by the intraperitoneal administration of 50 mg. (or more, if necessary) of sodium amytal per kilogram of body weight. A tracheal cannula was tied in place, and artificial respiration instituted by means of a motor-driven bellows. The chest was then opened by cutting the ribs bilaterally in the anterior axillary line. The sternum, with attached rib fragments, was thrown back, giving full exposure of the anterior part of the thorax. The peri-

cardium was opened from apex to base and fixed against the lateral chest walls without altering the position of the heart, but allowing free access to all portions of its surface. Only acute experiments were undertaken.

The indifferent electrode in all experiments was a needle electrode inserted into the muscle of the right forepaw. The exploring electrode used to obtain the potential variations of the ventricular cavity was a needle, insulated by baked enamel to within 5 mm. of the tip. Epicardial as well as precordial tracings were obtained with an exploring electrode consisting of a metal shaft, insulated by rubber tubing except at the end, where it was covered with several thicknesses of gauze kept well saturated with warm 0.85 per cent sodium chloride solution. Electrocardiographic results were continually visualized during the experiments by means of a Sanborn cardioscope, and, at appropriate points, tracings were made for permanent records with a Sanborn amplifying type of electrocardiograph.

In almost all experiments, after opening the pericardium and before manipulating the heart, the T waves in direct and semidirect leads, particularly in tracings made over the left ventricle, were found to be inverted, probably because of exposure of the heart to relatively cool air. This phenomenon has been discussed previously by Barnes and Mann.[23] The RS-T segment, however, was usually not significantly displaced, thus allowing satisfactory control tracings for our purposes.

Realizing that slight pressure or friction of an electrode on the underlying cardiac tissue will cause RS-T segment displacement, due caution was observed in the application of the electrodes. This appeared to be especially important when taking tracings from the ventricular cavity. Unless (1) all of the uninsulated tip of the needle electrode was inserted beyond the endocardium and into the ventricular cavity, and (2) contact with the endocardial wall was avoided, RS-T segment elevation was always present. The utmost precautions are therefore required to exclude artifact as a cause of RS-T segment displacement recorded with an electrode in a ventricular cavity. Negative displacement was never recorded in control tracings.

In certain instances, more than one type of experiment was performed on the same heart. However, prior to each experiment, the heart was allowed to return to its original state, at least as far as tracings were concerned, and preliminary control tracings were always made. Each type of experimental observation was carried out on one or more previously unmanipulated hearts.

Types of Experiments and Results.—

I. The epicardial surface of the heart was bathed in warm fifth-molar potassium chloride solution in three animals. Tracings were taken from all parts of the surface of both ventricles and from the endocardial cavity of each ventricle. The changes were always of the same type, and consisted of positive RS-T segment displacement in leads with the exploring electrode anywhere over the outside of either ventricle (as had been anticipated from previous work by others with potassium chloride), in a pad lead from over the surface of the heart, and in Lead II. On the other hand, negative RS-T segment displacement was always recorded when the exploring electrode was inserted into the endocardial cavity of either ventricle (Fig. 1, *A* series). Washing the epicardium with warm 0.85 per cent sodium chloride solution then brought the RS-T segment rapidly back to the isoelectric line, whereupon irrigation of the

epicardium with potassium chloride again caused the previously-described segment displacements. This procedure could be repeated several times on the same heart with the same results. In one instance, bathing only the left ventricle with fifth-molar potassium chloride solution caused positive RS-T segment displacement in leads from the surface of that ventricle, and negative RS-T segment displacement from the surface of the right ventricle (Fig. 1, *B-1* and *B-2*). With the development of positive segment displacement, the amplitude of the intrinsic deflection of the QRS complex tended to decrease. As a rule, it extended little, if at all, toward the base line beyond the level of the RS-T segment. The pre-intrinsic deflection was practically uninfluenced by the external application of potassium chloride solutions. The T wave tended to change from the inversion recorded in controls to the upright position.

A single experiment was carried out in which the external surface of the heart was bathed in an extremely dilute solution of ouabain. This produced positive RS-T segment displacement in leads from the epicardial surface which, over the course of several minutes, became quite marked (Fig. 1, *C-1* and *C-2*). The pattern was quite different from that produced by potassium chloride, in that the amplitude of the intrinsic deflection was but little affected, the positive RS-T segment displacement which was maximum at the end of the QRS complex decreased rapidly, and the T wave remained inverted. Negative RS-T segment displacement was recorded when an exploring needle electrode was placed within the left ventricular cavity (Fig. 1, *C-3*). This pattern was different from that produced in the ventricular cavity by the external application of potassium chloride solution, in that the negative displacement which was maximum at the end of the QRS complex diminished rapidly.

II. Injection of fifth-molar potassium chloride solution into the ventricular wall was carried out on two animals. A 20-gauge needle was introduced into the myocardium at an acute angle, and plunged to a point which was thought to be subendocardial. That it was in fact subendocardial was confirmed by post-mortem examination of the heart. Injection of 1 to 2 c.c. of the potassium chloride solution then produced marked negative RS-T segment displacement in leads taken from regions of the epicardium overlying the point of injection (Fig. 1, *D-1* and *D-2*). Continued injection led finally to positive RS-T segment displacement in leads from the same areas (Fig. 1, *D-3*). Injection of the potassium chloride solution into the subepicardial muscle, on the other hand, gave only positive RS-T segment displacement in leads from the overlying epicardium (Fig. 1, *D-4*). These changes were temporary, so that, after waiting a few minutes, the tracings assumed the form of the control tracings. Thereupon, reinjection of potassium chloride solution caused the appearance of the same phenomena. These experiments could be repeated as often as three times on the same heart with comparable results.

III. Scarification of the endocardium was carried out in four dogs. The technique on two animals was as follows: a small metal curette, on the end of a slender steel rod, was introduced through a small slit in the left auricular appendage (which was ligated about the rod to avoid blood loss), and passed down through the mitral valve into the left ventricular cavity. Control tracings were taken. Then injury was produced by turning the curette against the endocardium.

Injury to the endocardium of the left ventricle in one animal by the method described produced positive RS-T segment displacement in

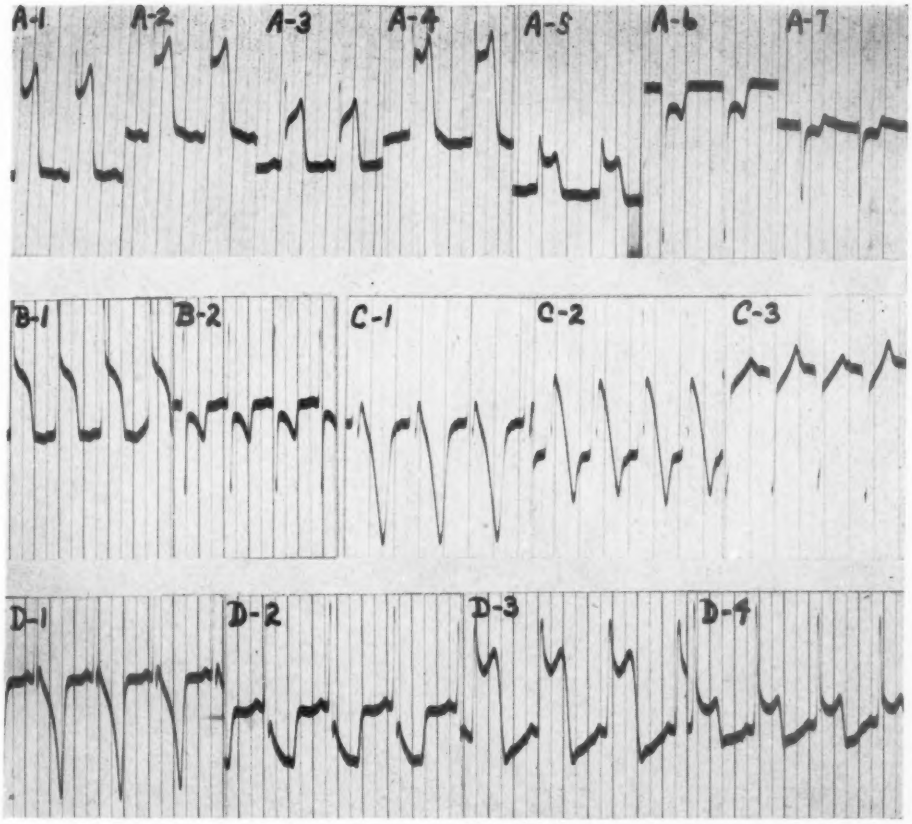


Fig. 1.—In all experiments the exploring electrode was paired with a needle electrode inserted into the right foreleg.

The *A* series illustrates the results of bathing the entire epicardial surface of the canine heart with fifth-molar solution of potassium chloride. The control tracings with the exploring electrode on the epicardial surface (not shown, but similar to Controls *A-1* to *A-7*, inclusive, Fig. 4) exhibited intrinsic deflections extending from the peak of the preintrinsic deflection to the neighborhood of the base line or below it, negligible RS-T segment displacement, and inverted T waves (as is common when the surface of the heart is exposed). In *A-1* an exploring electrode (covered with gauze and saturated with warm salt solution) was placed at the left ventricular apex, in *A-2* on the lateral wall of the left ventricle, and in *A-3* on the right ventricle near the apex. These illustrate the positive segment displacement obtained over the entire right and left ventricular surface. *A-4* is a pad lead. A large surgical gauze sponge, soaked with warm salt solution, was placed over the surface of the heart, and the exploring electrode was placed on the surface of the sponge overlying the left ventricle. *A-5* is Lead II. (In all leads, the sensitivity of the galvanometer was adjusted to display the pattern, so that amplitude of deflections cannot be compared.) *A-6* is a lead with an exploring needle electrode in the left ventricular cavity, and *A-7* is a similar lead, with the electrode in the right ventricular cavity. Negative displacement had not been present in the control endocardial leads.

In the *B* series the epicardial surface of the left ventricle, only, was bathed with fifth-molar potassium chloride solution. In *B-1*, the exploring electrode was placed on the anterior surface of the left ventricle and, in *B-2*, on the uninvolved surface of the right ventricle.

The *C* series illustrates results obtained by bathing the epicardial surface with a dilute solution of ouabain in salt solution. *C-1* is a control epicardial lead from the anterior wall of the left ventricle. *C-2* was obtained from the same area several minutes after the application of ouabain solution. The change in the RS-T segment and in the depth of T wave was gradual, and *C-2* represents the maximum change. *C-3* was made with a needle electrode in the left ventricular cavity. Note difference of ventricular patterns after application of potassium chloride solution and ouabain.

The *D* series illustrates effects of injection of fifth-molar potassium chloride solution into the ventricular wall. *D-1* is a control obtained from the epicardial surface of the anterior wall of the left ventricle. *D-2* was obtained from the same area after the injection of fifth-molar potassium chloride solution deep into the muscle underlying the electrode. *D-3* shows the effect of further injection into the same area, with probable infiltration of the solution toward the epicardium. *D-4* shows the initial effect of injection of fifth-molar potassium chloride solution in the subepicardial part of the muscle directly under the electrode. The control for this experiment was similar to *D-1*.

leads from within both ventricular cavities (Fig. 2, *A-1* and *A-2*). Leads taken at various points from the anterior, lateral, and posterior surface of both ventricles showed negative RS-T segment displacement in every instance. Post-mortem examination of this heart revealed two distinct areas of injury: one on the anterior endocardial wall of the left ventricle near the apex, measuring 8 by 8 mm., and another on the posterolateral endocardial surface, about 1 cm. square. At both points, only endocardium and the subendocardial muscle had been injured.

Endocardial damage, produced by the same method, to the left ventricle of another dog produced changes of the same type and degree as in the first animal. In addition, however, significant, negative RS-T segment displacement was recorded in Lead II, as well as in three precordial leads, namely, one taken from the right of the sternum, one from over the sternum, and one from the left of the sternum (Fig. 2, *A-3* to *A-12*, inclusive). It was further noted in this experiment that the degree and duration of the negative RS-T segment displacement seemed directly related to the extent of the endocardial injury. After slight injury, the negative RS-T segment displacement on the outside of the heart was of small magnitude and quite transitory, whereas, after more severe damage, the negative displacement was greater and more lasting.

Two earlier experiments of this same type were performed, using a different method of injuring the endocardial surface. The injury produced by this method was slight, and the tracings in these experiments were equivocal. It appears that fairly extensive trauma to the endocardial surface of the heart is necessary, when this method is used, to produce significant negative RS-T segment displacement on the epicardial surface, and therefore on the precordium. The rapid decrease in magnitude of the displacement in these experiments suggested that vascular spasm may have helped to produce it.

IV. Various portions of the epicardial surface of the hearts of four dogs were damaged by cautery, and leads taken from the area of injury, periphery of the injury, and from points on the surface of the heart quite distant from the injury. The technique followed was to heat the tip of an iron rod to redness, and then place it on a previously designated area of the epicardium. The area of damage was usually from 1 to 2 cm. square. Care was taken to sear only the most superficial portion of the subepicardial muscle. Although every effort was made to avoid injury to superficial blood vessels, it was not always possible to be sure that no arterial damage had resulted. Nevertheless, by this method one is able to produce a fairly well-defined area of injury.

The posterior wall of the left ventricle was damaged by this means in three animals. In the first of these experiments the area of injury was small. Leads taken from the damaged area showed positive RS-T segment displacement, whereas leads taken from other areas of the epicardium showed no significant RS-T segment displacement. The second experiment, however, in which the area of damage was larger (approximately 1 cm. square), revealed that, although leads taken from the seared area showed positive RS-T segment displacement, leads taken from normal-appearing epicardium at the periphery of the injured area on the lateral and posterolateral surface of the left ventricle showed negative RS-T segment displacement, and leads from the anterior wall of the left ventricle showed even greater negative RS-T segment displacement. In the third experiment of this sort, no RS-T segment displacement was obtained from the anterior wall of the left ventricle, but positive RS-T segment displacement occurred not only in leads from the

injured area, which was low on the posterior wall, but also in leads from the apex (Fig. 3, *A-5* and *A-6*). The latter may have been due to the fact that, in this experiment, a small superficial blood vessel was involved in the injury. However, at the periphery of the lesion on the lateral wall of the left ventricle, negative RS-T segment displacement appeared (Fig. 3, *A-7*). As one gradually moved the electrode from the injured area toward the lateral wall, the positive RS-T segment displacement decreased until the segment became isoelectric, and, finally, negative RS-T segment displacement appeared in leads from unseared tissue bordering on the area of injury (Fig. 3, *A-9*). This sequence of events occurred while moving the electrode not more than 1 centimeter. The zone in which negative RS-T segment displacement alone occurred was, however, considerably wider. The electrode was then placed just outside the burned area, in the zone where negative RS-T segment displacement was

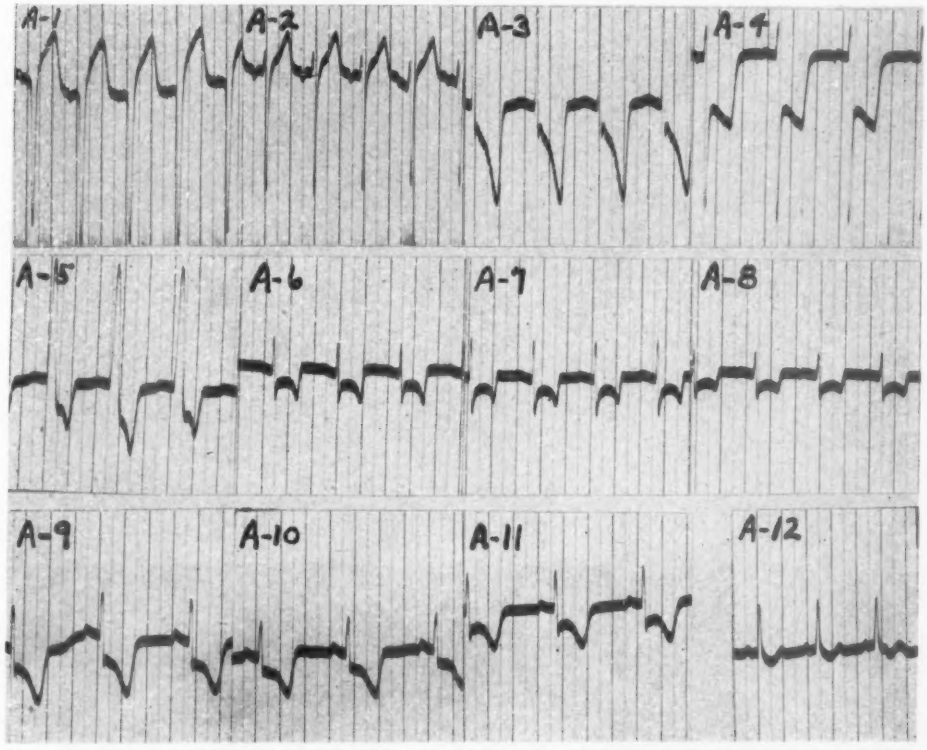


Fig. 2.—Electrocardiograms after extensive trauma to the endocardial side of the canine left ventricle, produced by means of a metal curette inserted through the left auricular appendage and mitral valve. The electrode paired with the exploring electrode was placed on the right foreleg.

A-1 and *A-2* were obtained with a needle electrode in the left and right ventricular cavities, respectively. The positive RS-T segment displacement in these leads is of doubtful significance because of the difficulty of excluding the possibility of contact of the needle with the ventricular wall as a cause of this displacement. In *A-3* the exploring electrode was placed on the epicardial surface of the apex of the left ventricle, in *A-4* on the anterior wall, and in *A-5* on the posterior wall. In *A-6* it was placed on the anterior wall of the right ventricle, in *A-7* over the lateral wall, and in *A-8* over the pulmonary conus. The anterior chest wall was then replaced. *A-9* was made with the exploring electrode on the left side of the anterior chest wall fourth intercostal space, *A-10* over the sternum at the same level, and *A-11* over the right side of the chest wall, fourth intercostal space. *A-12* is Lead II. The controls (not shown) had exhibited no significant segment displacement. The sensitivity of the galvanometer, as in Fig. 1, was adjusted to illustrate patterns, so that differences in amplitude are not comparable. The widened QRS complex in *A-5* suggests that a conduction tract to the posterior wall of the left ventricle was traumatized.

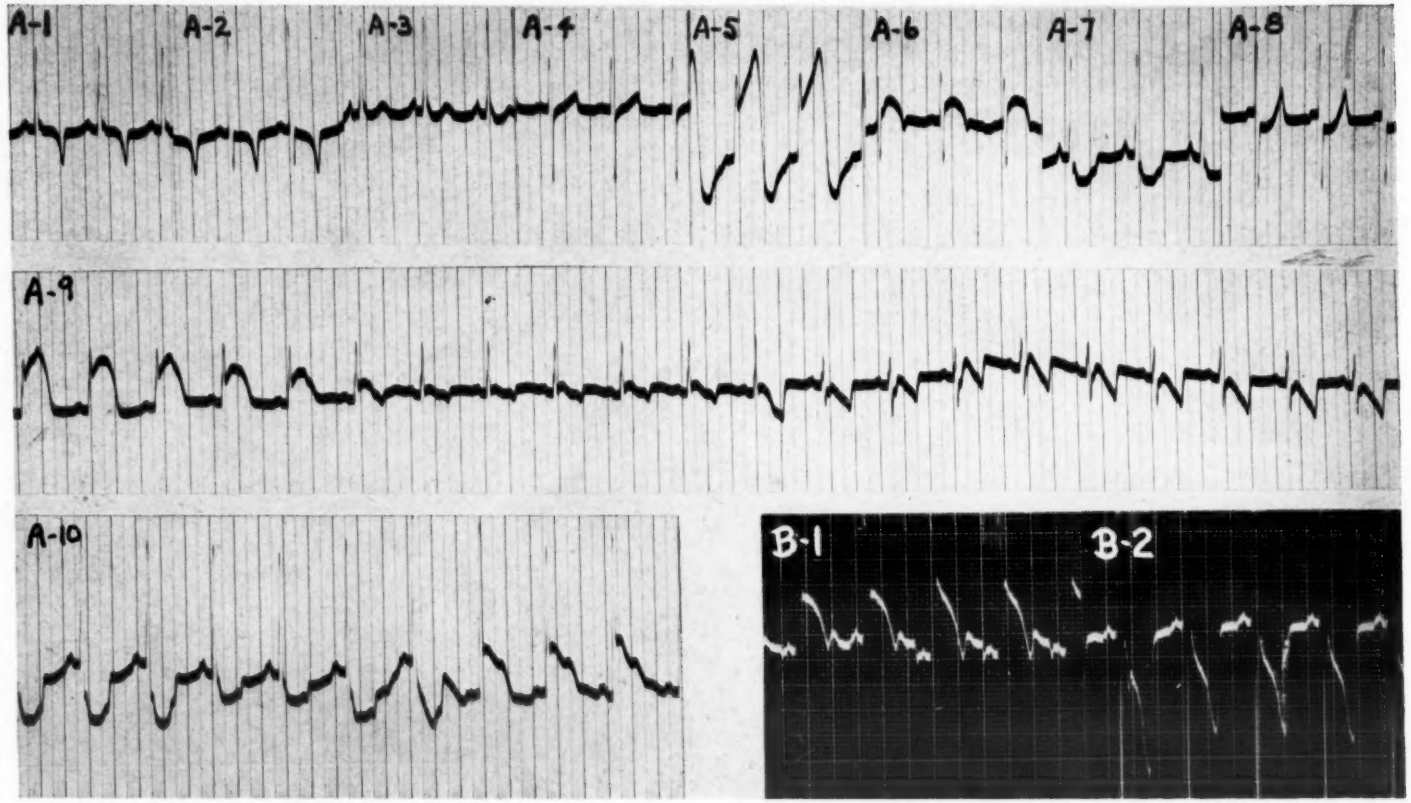


Fig. 3.—Results obtained by cauterization of localized epicardial areas. *A-1* to *A-4*, inclusive, are control epicardial leads. In *A-1* the exploring electrode was placed on the posterior wall of the left ventricle, in *A-2* on the left ventricular apex, in *A-3* on the lateral wall of the left ventricle, and in *A-4* on the lateral wall of the right ventricle. The posterior wall of the left ventricle was then cauterized; the area of the searing was roughly 2 cm. in diameter. In *A-5* the exploring electrode was placed directly over the cauterized surface at about the same position as in *A-1*. In *A-6*, the electrode was placed in the same position as in *A-2*, over presumably uninvolved muscle. This was the only instance in the entire study in which significant positive displacement was recorded over presumably uninvolved muscle. The possibility that the arterial supply to this region was damaged in cauterization could not be ruled out. In *A-7* and *A-8* the positions of the exploring electrode were the same as in *A-3* and *A-4*, respectively. In this experiment the sensitivity of the galvanometer was not changed. Note that in *A-1* and *A-5* the preintrinsic deflection remains about the same, but the intrinsic deflection is greatly reduced in amplitude. The direction of the T wave also changes.

In *A-9* the exploring electrode was slowly moved from the surface of a cauterized area on the anterior wall to a position about 2 cm. beyond the area of injury. In *A-10* the exploring electrode was slowly moved from a point about 1 cm. outside a cauterized area back onto its surface. The more abrupt change in the direction of segment displacement in *A-10* is not due to more rapid movement of the exploring electrode.

In *B-1* the exploring electrode was placed over a cauterized area on the posterior wall of the left ventricle, and in *B-2* on the anterior wall of the same ventricle.

recorded. Moving the electrode only a few millimeters toward the burned area caused an abrupt change from negative to positive displacement (Fig. 3, *A-10*).

The anterior epicardial surface of the left ventricle was seared in one animal. Positive RS-T segment displacement was recorded from the injured area, and negative displacement in leads from the posterior wall of the right ventricle (Fig. 3, *B-1* and *B-2*). The changes in ventricular pattern obtained by placing an exploring electrode over a cauterized area are similar to those which follow the application of potassium chloride solution to an epicardial area, not only with respect to segment displacement, but the intrinsic deflection and the T wave, as well.

V. The effect on six animals of complete occlusion of a coronary artery, either by clamp or ligation, was studied. The posterior descending portion of the circumflex branch of the left coronary artery was occluded in four instances, and the anterior descending branch of the left coronary artery in two.

Occlusion of the posterior descending artery resulted in marked positive RS-T segment displacement in leads from that portion of the posterior wall of the left ventricle which was deprived of its blood supply, as well as in Lead II. Leads from the lateral wall of the left ventricle, just peripheral to the area deprived of blood supply, as well as leads from the anterior wall of the left ventricle, showed negative RS-T segment displacement in three of the four experiments (Fig. 4, *A-1* to *A-16*, inclusive). It was possible in one of these experiments to demonstrate an abrupt change from positive to negative displacement by moving the electrode only a few millimeters from the area of ischemia to normal-appearing tissue on the lateral wall of the left ventricle (Fig. 4, *A-17*). In this same experiment, a pad lead taken from the anterior wall of the left ventricle showed negative RS-T segment displacement, as did leads from the surface of both auricles (Fig. 4, *A-18*). Another of this group of experiments gave rise to negative displacement in leads from the anterior and lateral walls of the right ventricle, as well as from the anterior and lateral walls of the left ventricle.

Occlusion of the anterior descending branch of the left coronary artery produced positive RS-T segment displacement in leads from the area of ischemia on the anterior wall of the left ventricle, and, in one instance, from a small portion of the anterior wall of the right ventricle bordering on the interventricular septum. Leads from the posterior wall of the left ventricle showed negative displacement (Fig. 4, *C-1*, *C-2*, and *C-3*), whereas Lead II failed to show significant displacement in either direction. In no instance was it possible to demonstrate significant displacement of the RS-T segment in either direction in leads from within the left ventricular cavity (Fig. 4, *B-1* and *B-2*). The ventricular patterns obtained by placing an exploring electrode on the epicardial surface of a part of the heart muscle which was completely deprived of blood supply were much like those obtained after cauterization or the application of potassium chloride solution. However, at the margin of such a region the amplitude of the intrinsic deflection was relatively little decreased, even though pronounced positive RS-T segment displacement might be present.

VI. Partial occlusion of a coronary artery, produced by various methods, was the object of three types of experiments.

A. In one animal, a small segment of the anterior descending branch of the left coronary artery was dissected free, and control tracings were taken. A slender metal rod was placed alongside the artery, and a liga-

wall of the same ventricle. electrode was placed over a cauterized area on the posterior wall of the left ventricle, and in *B-2* on the anterior

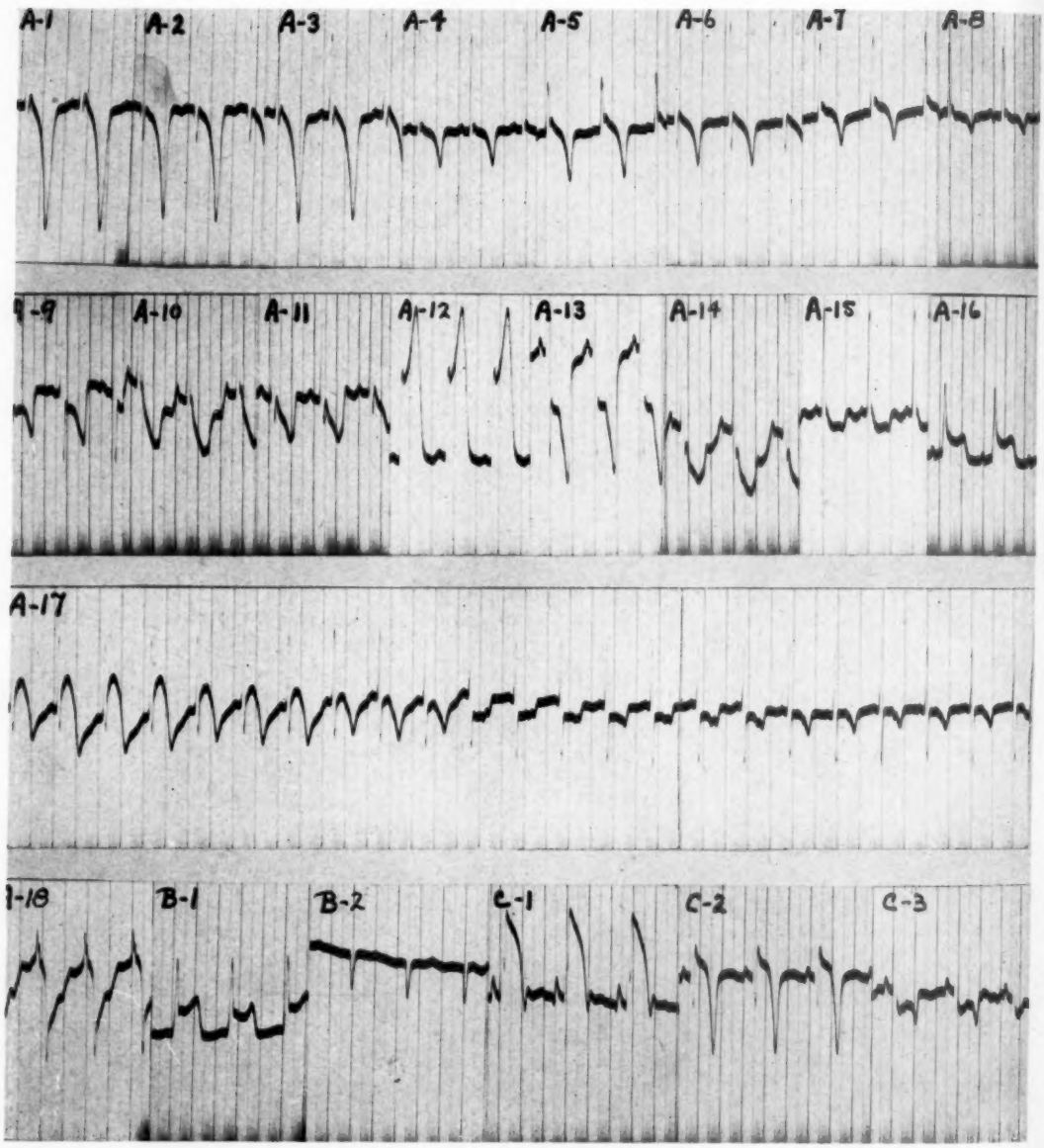


Fig. 4.—*A-1* to *A-8* are control tracings made just prior to complete obstruction of the posterior descending branch of the left circumflex artery. In *A-1* the exploring electrode was placed on the epicardial surface of the anterior wall of the left ventricle, in *A-2* on the apex, in *A-3* on the lateral wall, in *A-4* on the posterior wall, in *A-5* on the anterior wall of the right ventricle, in *A-6* on the lateral wall, and in *A-7* on the posterior wall. *A-8* is Lead II. The artery was then obstructed. *A-9*, *A-10*, *A-11*, and *A-12* were made with the exploring electrode in approximately the same positions as *A-1*, *A-2*, *A-3*, and *A-4*, respectively. In *A-13*, the exploring electrode was on the anterior wall of the right ventricle near the base, and in *A-14* on the posterolateral wall of the right ventricle. *A-15* was a pad lead; a large, moistened, surgical sponge was placed over the anterior surface of the heart, and the exploring electrode was placed on the sponge over the left ventricle. *A-16* is Lead II. In *A-17*, the exploring electrode was moved slowly from what was regarded as the margin of the area of disturbance of arterial blood supply to presumably unin-

(Continued on opposite page.)

ture was drawn tight about both rod and artery and tied. The rod was then gently pulled from beneath the ligature, leaving partial compression of the artery. This procedure was repeated, using next a no. 19 needle and finally a no. 24 needle in place of the rod. In all three instances the immediate effect was RS-T segment elevation in leads from the area partially deprived of its blood supply. Immediately after removal of the ligature, negative RS-T segment displacement which was quite transitory, lasting only a minute or two, appeared in leads from the same area where previously RS-T segment elevation had been seen (Fig. 5, *A-1* and *A-2*).

B. A modified Goldblatt clamp was placed about the anterior descending branch of the left coronary artery of another animal, and control tracings were taken. Then gradually increasing pressure was applied to the artery. The primary change was always positive RS-T segment displacement in leads from the ischemic area, with negative RS-T segment displacement in leads from the lateral wall peripheral to this area. After releasing the pressure on the artery, again an immediate, but transitory, negative RS-T segment displacement was seen in leads from the previously ischemic area.

The clamp was applied to the circumflex branch of the left coronary artery in this same animal, and again the primary change was always positive RS-T segment displacement, this time over the posterior and lateral aspects of the left ventricle supplied by this artery, with negative RS-T segment displacement on the anterolateral and anterior walls of the left ventricle and the anterior and lateral walls of the right ventricle. Removal of the arterial compression was followed, as before, by transitory negative displacement in leads from the area where previously positive displacement had been recorded.

C. A fine thread was passed beneath the anterior descending branch of the left coronary artery of a third dog. Progressively increasing traction was applied to the artery by pulling the thread, thus gradually decreasing its lumen. The primary effect was negative RS-T segment displacement in leads from the area whose blood supply was impaired, i.e., the anterior wall of the left ventricle (Fig. 5, *B-1* and *B-2*). Increasing the traction further led to positive displacement in leads from the same area (Fig. 5, *B-7*), and, finally, release of traction altogether gave rise, after a short interval, to transitory negative displacement in leads from the previously ischemic area. During the period that negative displacement was recorded from the surface of the area partially deprived of blood supply, positive displacement was recorded nowhere over the surface of the left ventricle (Fig. 5, *B-3 B-4*, and *B-5*). However, over the anterolateral surface of the right ventricle at some distance from the area of interference with blood supply, slight positive displacement was recorded, although no more than was often noted in controls (Fig. 5, *B-6*).

---

volved tissue. Note that the intrinsic deflection is preserved in *A-17*, whereas it is almost lost in *A-12*. Positive RS-T segment displacement changed gradually to negative displacement as the electrode was moved away from the area of involvement. Finally, an area was reached where there was no significant segment displacement. In *A-18* the exploring electrode was placed on the left auricle. The ventricular QRS pattern at that position was of the endocardial type, but the significance of the negative RS-T segment displacement is uncertain.

B-1 was made with the exploring electrode on the anterior wall of the left ventricle after complete obstruction of the anterior descending branch of the left coronary artery. Despite the positive displacement in that lead, no segment displacement was recorded in *B-2*, in which the needle electrode was placed in the left ventricular cavity.

In the *C* series (another preparation), the anterior descending branch was also ligated. *C-1* was obtained with the exploring electrode on the anterior wall of the left ventricle, *C-2* at the apex, and *C-3* on the uninvolved posterior wall of the left ventricle.

An attempt was made to repeat the above experiment on two other dogs, using the anterior descending branch of the left coronary artery. In neither case were we able to obtain negative displacement over the area partially deprived of blood supply during the time the artery was partially obstructed, although positive displacement was readily obtained. Under these circumstances, however, negative displacement could be recorded from adjacent areas. It could also be recorded from

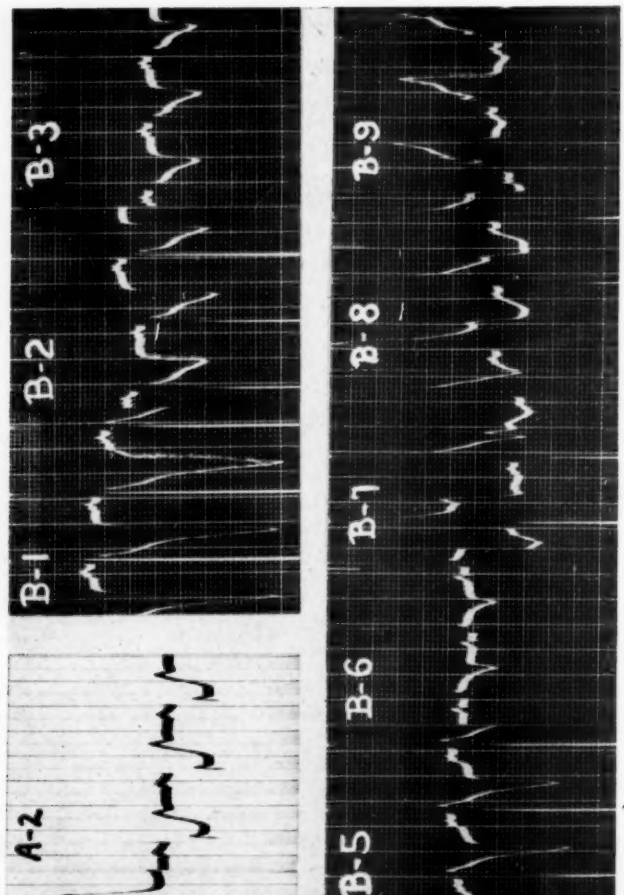


Fig. 5.—Results obtained by partial occlusion of a coronary artery.
In *A-1*, the anterior descending branch of the left coronary artery had been partially occluded by manual traction on a thread passed under the vessel. The exploring electrode was placed on the anterior wall of the left ventricle in the area of distribution of the vessel. In this instance, in spite of very gradual increase in the degree of traction, the initial change in the RS-T segment was positive displacement. Note that the intrinsic deflection was preserved. After release of traction, the direction of segment displacement in the same area became negative, as shown in *A-2*, prior to the return to the pattern obtained before the beginning of the experiment.
The *B* series illustrates the only experiment in which negative displacement was recorded from the epicardial surface without preceding or accompanying significant positive displacement, after partial obstruction of a coronary artery. Similar results were obtained three times in this preparation. *B-1*, a control tracing made with an exploring electrode on the anterior wall near the apex (after dissection of a part of the anterior descending branch of the left coronary artery free from surrounding structures and the insertion of a thread under it), showed slight negative displacement. In *B-2*, made from the same position after slight traction on the thread, the initial change was an increase of the negative displacement, and less deep inversion of the T wave. In *B-3* the exploring electrode was placed posteriorly on the left ventricle near the apex, in *B-4* on the lateral wall, in *B-5* anteriorly at the septum, and in *B-6* over the anterior surface of the right ventricle. The slight positive displacement recorded in *B-6* was no more than is sometimes found in controls. Traction on the artery was then increased. In *B-7*, *B-8*, and *B-9* the position of the exploring electrode was the same as in *B-2*, *B-4*, and *B-5*. Note that in all these positions negative displacement was converted to positive displacement by complete obstruction of the artery.

the area partially or fully deprived of blood supply after release of pressure on the vessel, provided positive displacement had been present during the period of pressure. When positive segment displacement was recorded with an exploring electrode at an epicardial surface after partial deprivation of blood supply to the underlying muscle, the intrinsic deflection, like that recorded from near the margin of a region completely deprived of blood supply, was but little decreased in amplitude.

VII. Miscellaneous observations. During the course of the experiments described above, it was noted that negative potential change during the RS-T interval, produced over the surface of uninvolved muscle by involvement elsewhere, could be converted to positive change by the direct application of potassium chloride solution or by deprivation of the arterial blood supply to the underlying muscle (Fig. 6, *D* series).

The application of fifth-molar lithium lactate solution or fifth-molar lithium citrate solution to an epicardial surface produced, at most, slight positive RS-T potential change. One hundredth-molar potassium chloride solution, however, produced immediate positive displacement comparable to that caused by the fifth-molar potassium chloride solution used in the experiments described above (Fig. 6, *A-1* and *A-2*). The application of fifth-molar calcium chloride solution to an epicardial surface produced positive change, but it was much less in magnitude than

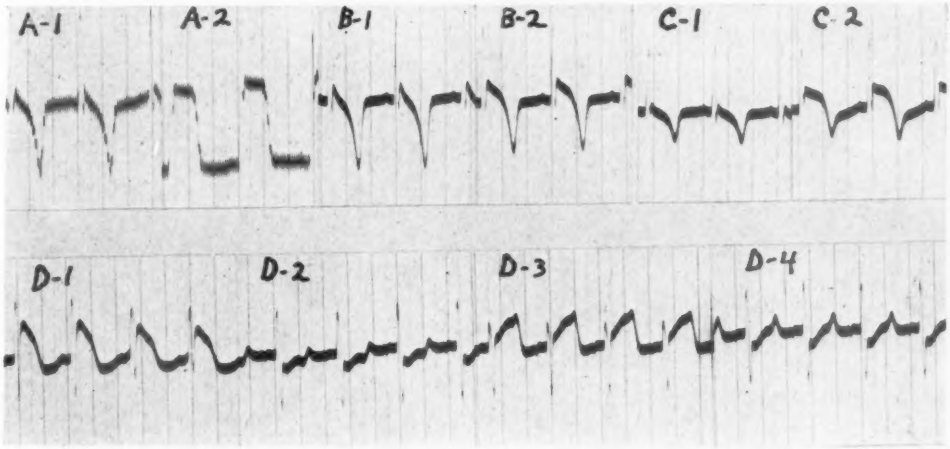


Fig. 6.—*A-1* is a control tracing made with an exploring electrode on the anterior surface of the left ventricle. *A-2* was obtained from the same area less than one minute after the application of one hundredth-molar potassium chloride solution.

B-1 is a control from the same area after repeated washing with warm salt solution. *B-2* shows the maximum change observed after the application of fifth-molar calcium chloride solution to this area.

C-1 is a control tracing from the lateral wall of the left ventricle. *C-2* shows the maximum change obtained from the same region after the application of fifth-molar calcium chloride solution.

In *D-1* the exploring electrode was placed on the posterior wall of the left ventricle after application of a dilute solution of epinephrine to that region. In *D-2*, which was made immediately after *D-1*, the exploring electrode was placed on the anterolateral wall of the left ventricle, which had not been exposed to epinephrine. *D-3* was made from the same general area as *D-2*, after temporary obstruction of blood supply to that region. *D-4* was made after release of obstruction. Note the differences in pattern produced by potassium chloride, calcium chloride, and epinephrine solutions, and the fact that secondary negative segment displacement obtained over uninvolved areas can be converted to positive displacement by obstruction of blood supply to that region.

that produced by one hundredth-molar potassium chloride solution (Fig. 6, *B* and *C* series). The displacement in leads from such areas was sustained longer than that produced by ouabain, but not as long as that produced by potassium chloride. The intrinsic deflection was but little affected. The magnitude of the inverted T wave of the control tracing was lessened, but its direction was not changed. Extremely dilute solutions of epinephrine produced positive displacement in leads over the area of application, and negative displacement elsewhere. The displacement, like that produced by applying calcium chloride solutions, was

less sustained than that which followed the application of potassium chloride deprivation of blood supply, or cauterization.

In a case of hypertensive disease in which there was negative RS-T segment displacement in Lead II and chest leads CR_3 to CR_6, inclusive, an esophageal lead (exploring electrode paired with an electrode over the spine of the right scapula), made with the exploring electrode below the auricular level, also exhibited negative RS-T segment displacement. However, when the exploring electrode was moved to the auricular level

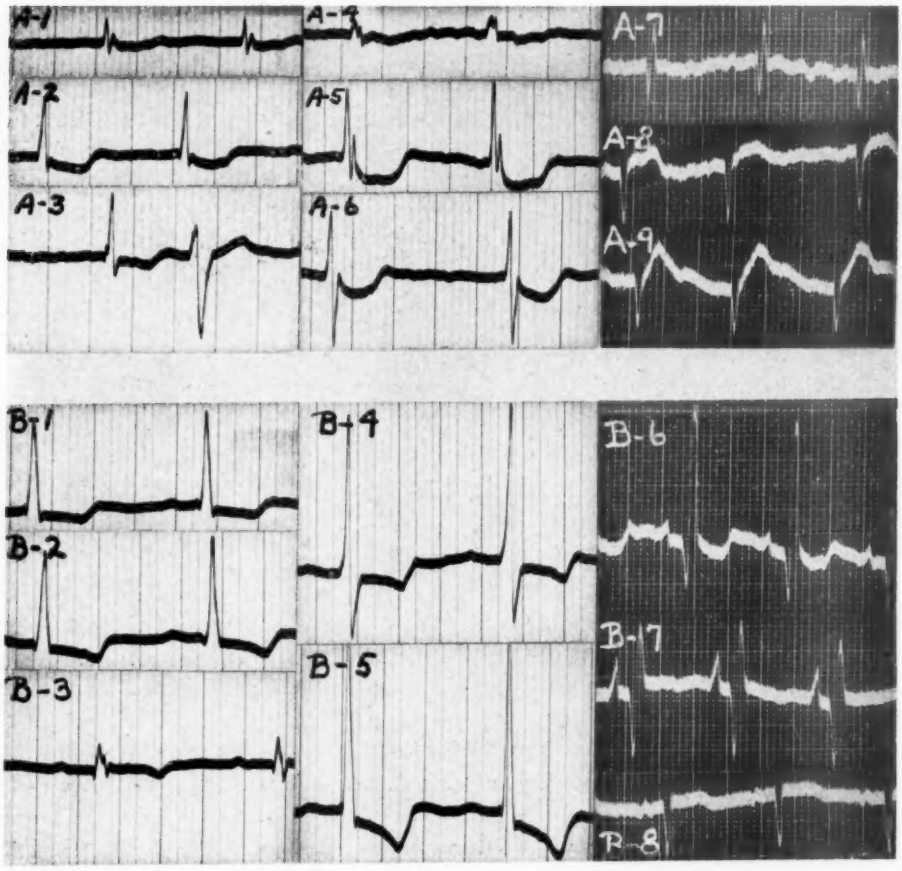


Fig. 7.—The *A* series was obtained from a patient with mitral stenosis, auricular fibrillation, low blood pressure, and no demonstrable left ventricular enlargement. He had been taking digitalis in a dose of 1½ to 3 grains daily to keep the ventricular rate under control. *A-1*, *A-2*, and *A-3* are Leads I, II, and III, respectively, and *A-4*, *A-5*, and *A-6* are leads CR_1, CR_2, and CR_6, respectively. *A-7* was made with the exploring electrode in the esophagus slightly below the auricular level, *A-8* at the auricular level, and *A-9* slightly above the auricular level. The QRS pattern is of the endocardial type in *A-8* and *A-9*, positive RS-T segment displacement is present in *A-8*, in contrast to body surface leads, and the T wave is abnormally upright in *A-8* and *A-9*.

The *B* series was obtained from a patient with hypertension and left ventricular hypertrophy. Digitalis had not been administered. *B-1*, *B-2*, and *B-3* are Leads I, II, and III, respectively. *B-4* and *B-5* are leads CR_2 and CR_5 respectively. In *B-6*, the exploring electrode was in the esophagus below the auricular level, in *B-7*, at the auricular level, and in *B-8* slightly above the auricular level. Note the change in RS-T segment displacement from slightly negative to slightly positive as the exploring electrode is moved from below the auricular level to that region and above. In this case the pure endocardial type of QRS complex was not obtained until the exploring electrode was slightly above the auricular level.

or to a position slightly above it, positive RS-T segment displacement was recorded (Fig. 7, *B* series).

The electrocardiogram of a well-digitalized patient with mitral stenosis and auricular fibrillation, but without hypertension or demonstrable left ventricular hypertrophy, showed negative RS-T segment displacement in Lead II and the chest leads, but exhibited positive displacement in a lead made with the exploring electrode at the auricular level of the esophagus (Fig. 7, *A* series).

DISCUSSION

One of the important unsolved problems of electrocardiography concerns itself with the physicochemical mechanism or mechanisms responsible for RS-T segment displacement. The solution of this problem would probably constitute a significant advance toward a clearer understanding of the bioelectric phenomena responsible for electrocardiographic deflections in general. The work of Osterhout[24] with nitella cells and his model of the potassium effect emphasize the importance of change in the permeability of the cell membrane, the migration of K^+ ions to the outer surface of the cell membrane during excitation, and the presence of the "R" substance as essential factors in the development of potential changes. Possibly similar phenomena are concerned in the excitation of heart muscle fibers, although the part that they may play in the development of the changes in potential which are responsible for the electrocardiogram is not as yet known.

During the course of this study, although our interest was focused on the distribution of pathologic positive and negative RS-T segment displacement, the qualitative differences in ventricular patterns produced by some of the experimental procedures described above were so striking that they could scarcely escape notice.

In the analysis of these patterns the behavior of the intrinsic deflection and T wave, as well as the RS-T segment, requires consideration. However, one need only observe the differences in the characteristics of the segment displacement produced by the application of potassium, calcium and ouabain solutions to realize that the theoretical explanations offered in the past as to its nature are not adequate. One point, at least, seems clear: the RS-T segment cannot under all circumstances be merely the reflection of continuous current flow during diastole, as would be the case if it were due solely to incomplete repolarization. Its characteristics must be determined, at least to some extent, by what takes place or fails to take place during systole.

Electrocardiography owes a great debt to Lewis and his collaborators[25] for the differentiation between the intrinsic deflection of the QRS complex and the deflections of extrinsic origin. The intrinsic deflection, according to Lewis' views, reflects the sharp fall in potential at the part of the surface of the heart in contact with an electrode at the onset of

excitation of the muscle fibers directly under that surface. All other changes in potential transmitted to the electrode during the QRS complex represent electrical activity elsewhere, and are therefore classed as extrinsic. Obviously, in all parts of the ventricles except the part activated first, the intrinsic deflection cannot be recorded apart from potential variation caused by extrinsic electrical activity. Nevertheless, the intrinsic deflection is easily recognized, although it is subject to distortion, depending upon the extrinsic effects which occur at the same time. This distortion of the intrinsic deflection, however, does not impair the usefulness of the concepts developed by Lewis regarding the QRS complex. It seems to us, on the basis of the observations reported above, that the concept of differentiation between intrinsic and extrinsic effects can be extended with advantage to the RS-T segment. The possibility exists that it may also be useful in the case of the T wave. However, in order to avoid confusion in nomenclature, we shall use the terms primary and secondary instead of intrinsic and extrinsic. By RS-T segment displacement of primary type we mean displacement resulting from abnormal physicochemical disturbance in the muscle fibers directly under the electrode. By displacement of secondary type, we mean the displacement that can be recorded over the surface of uninvolved muscle; the potential change is induced at that surface by involvement elsewhere.

The RS-T segment possesses advantages over the QRS complex and the T wave for the study of potential change of what we call primary and secondary type. In the first place, if suitable precautions are taken, RS-T segment displacement recorded over the surface of healthy heart muscle is so small in magnitude, compared with that which can be produced by experimental procedures, that it can be disregarded. Second, the region in which RS-T segment displacement is produced experimentally can be localized so accurately in certain types of experiments that, except at the margin of the area of involvement, one can be confident that he is dealing either with primary or secondary effects, and not with a mixture of both.

In the experimental results reported above, the primary RS-T segment potential change, with one possible exception, which will be discussed below, was always positive, and the secondary change, wherever it occurred, was always negative. Thus, positive potential change produced at the epicardial surface by local disturbance caused negative displacement in leads from the endocardial cavities; acute trauma to the endocardial side of the heart wall produced negative displacement from the uninvolved epicardial surfaces; positive potential change produced by the application of certain chemical solutions or cautery to a part of the epicardial surface produced negative potential change at other uninvolved epicardial surfaces. Complete obstruction of blood supply to one part of the heart wall, producing positive RS-T segment

displacement in leads with the exploring electrode over the surface of such an area, caused widespread negative displacement in leads from uninvolved areas.

As far as we are aware, it has not been demonstrated that negative RS-T segment potential changes can be produced at a cardiac surface by direct involvement of the fibers just under that surface. Whether the negative displacement observed once in this study after partial obstruction of a vessel, or the negative displacement recorded during the recovery period following positive displacement, is a primary effect, and reflects involvement of the fibers under the electrode, or is a secondary or induced effect resulting from positive potential change in the deeper layers of the heart wall, was not ascertained in these experiments. The latter explanation, however, seems more likely.

The results of these experiments, we believe, have a bearing on the interpretation of the patterns of RS-T segment displacement in human electrocardiograms. It appears safe to say that abnormal positive displacement in a chest lead reflects involvement of fibers at the epicardial surface, or near the surface underlying the exploring chest electrode. It is well known that there is a tremendous decrement in potential variation between an epicardial surface and the overlying precordial surface, which introduces a quantitative difference between leads made with the exploring electrode on each of these surfaces. This, however, is not so important in interpretation as the qualitative difference in patterns caused by essential differences in the relationships of electrode to parts of the epicardial surface. In an epicardial lead, the pattern of potential variation of the exploring electrode almost certainly depends on the mean potential variation at each instant of that part of the surface in direct contact with the electrode. In the case of the RS-T segment, such variation may be primary or secondary, or a combination of both. If the change from one type to the other in adjacent areas is abrupt, such distribution should be demonstrable by exploration with an electrode which has a small area of contact with the epicardium. That this is the case is strikingly illustrated by the experiments in which the electrode was slowly moved across the margin of an area of involvement and the abrupt change from positive to negative displacement observed. Such sudden changes cannot be obtained by exploring positions equally near each other on the chest wall. The reason for this is that an electrode with a comparable area of contact on the chest wall must necessarily tap the potential variations of a much larger epicardial area; the influence of each unit area on the electrode doubtless depends on the properties of the electrical pathway between that area and the electrode. Thus, if an acute lesion involves the anterior surface of the left ventricle, an exploring electrode placed on the chest wall over the right ventricle will, in all probability, have transmitted to it secondary negative potential derived from currents at the surface of that ventricle, and

primary positive potential from the surface over the lesion. The direction of segment displacement may therefore be upward or downward, depending upon which effect dominates.

If the exploring electrode is paired with one placed on a surface position which has relatively slight potential variation, such as over the spine of the right scapula (or even the right arm), positive RS-T segment displacement of magnitude sufficient to be abnormal in any precordial lead means that a part of the myocardium just beneath the epicardial surface, presenting toward the electrode, is involved. Negative displacement, on the other hand, signifies one of the following: (1) If the involvement extends to the ventricular epicardial surface, that part of the surface does not lie directly under the electrode, but might be situated anywhere outside the zone near the electrode, where involvement could dominate the direction of displacement. (2) Involvement limited to the endocardial aspects of the wall produces negative displacement, even when the site of injury underlies the electrode directly. (3) Partial deprivation of blood supply in the region directly underlying the electrode can produce negative displacement, although, as stated above, this may be a secondary effect caused by the production of positive displacement on the endocardial side.

In Lead II, or a lead in which the electrode on the leg is paired with one placed over the spine of the right scapula in order to minimize interference with the potential variations of the left leg, abnormal positive RS-T segment displacement indicates that the lesion involves a subepicardial region in close relationship with the diaphragm. Negative displacement, on the other hand, signifies (1) that the lesion involves some other part of the surface, (2) that the lesion is limited to the endocardial aspect of the wall not reaching the subepicardial region, or (3) that there is merely a partial deprivation of blood supply in some part of the heart.

The direction of potential variation during the RS-T interval in the esophagus well below the auricular level is the same as that of the left leg, and therefore adds no information of value regarding the segment. At the auricular level, however, the potential of the exploring electrode probably reflects the potential variations of the left ventricular cavity,[26] so that positive segment displacement signifies involvement of the endocardial aspects of the left ventricular wall. Our inability to obtain displacement in leads from the left ventricular cavity after occlusion of coronary arteries was unexpected. We finally concluded that positive potential change might have been counterbalanced by secondary negative change at uninvolved areas, so that the two tended to neutralize each other.

The experiments reported above explain why RS-T segment displacement in acute lateral infarction has the characteristics described by Wood, Wolferth, and Bellet,[17] in 1938. Negative RS-T segment deflection is recorded in precordial leads and in Lead II in lateral infarction

because the lesion is located in such a position that secondary negative displacement over the anterior surface of the heart and over the part of the heart in contact with the diaphragm governs the direction of segment displacement in those leads. If it were possible to place an electrode directly over the area of involvement, as can be done in experimental animals, primary positive displacement would doubtless be recorded if the lesion extended close to the epicardial surface. If, however, anoxemia also involves the anterior or diaphragmatic surface of the heart, this part of the lesion will dominate the direction of RS-T segment displacement in anterior chest leads and Lead II, respectively.

In the paper on lateral infarction, the close resemblance between the patterns of displacement produced by that lesion and a digitalis effect was pointed out. The recent illuminating studies by Barnes and his colleagues[27] indicate that digitalis effects are exerted preponderantly on the endocardial side of the cardiac wall, and that changes produced by prolonged anoxemia are also located on the endocardial side. Our experiments, as has been pointed out, have indicated that endocardial lesions produce the secondary type (negative) of potential change at epicardial areas. Consequently, it is probably not possible to distinguish, in body surface leads, the patterns of RS-T segment displacement which result from a lesion on the lateral wall of the left ventricle, even though it involves the epicardial surface, from one which involves the endocardial side of the ventricular wall, unless large conduction tracts become involved in the endocardial lesion. To what extent the direction of segment displacement obtained with an exploring electrode in the esophagus at the auricular level may help to clarify this situation will have to await further data. In the case of digitalis effect, the positive displacement recorded from the appropriate levels in the esophagus is in harmony with Barnes' observation that the digitalis effect is primarily on the endocardial side. Thus, the negative displacement recorded in the body surface leads is presumably of the secondary, or induced, type. The results of bathing the epicardial surface with a solution of ouabain, after which the direction of RS-T segment displacement is the opposite of that which occurs after administration of digitalis by mouth or parenterally, are also in accord with this concept. In view of the fact that the relationships of positive and negative segment displacement are the same in cases of hypertension as with digitalis effect, it seems probable that the source of the disturbance responsible for segment displacement is on the endocardial side, and that the negative displacement recorded in body surface leads likewise reflects negative displacement of secondary type at epicardial surfaces.

In order to reach a more complete understanding of RS-T segment displacement, a far more extended study, of partial deprivation of blood supply than the exigencies of the times have permitted us to make is necessary. However, from the practical viewpoint, it makes little difference whether the negative displacement recorded after partial de-

privation of blood supply is primary or secondary in origin. We have long been puzzled by the fact that, during an attack of angina pectoris, the electrocardiogram usually shows negative RS-T segment displacement, and thus resembles the pattern of acute lateral infarction. It did not seem reasonable to suppose that angina pectoris is usually accompanied by deprivation of blood supply to the lateral wall of the left ventricle alone. However, if the true explanation for the negative displacement observed during attacks of angina pectoris is anoxemia of the endocardial aspect of the wall, the electrocardiogram would exhibit negative displacement, irrespective of the artery or part of the heart affected. The negative displacement recorded in certain cases of shock, carbon monoxide poisoning, advanced coronary insufficiency without actual infarction, and even the hyperventilation syndrome could be easily accounted for by assuming selective involvement of the endocardial side of the heart wall. The evidence for this view, however, is not complete. Further study of partial deprivation of blood supply may throw more light on the problem. The facility of occurrence of negative RS-T segment displacement clinically, under circumstances of presumed oxygen want, and the difficulty we have experienced in trying to produce it experimentally, with the exploring electrode directly over the area of involvement, by partial obstruction of an artery, are not as yet completely reconciled.

It now seems likely that the negative RS-T segment displacement sometimes recorded in precordial leads early in the course of an attack of acute coronary occlusion, which later develop the typical pattern of infarction of the anterior wall, with positive segment displacement in the same leads, reflects a state of partial deprivation of blood supply prior to complete occlusion. The same explanation may apply in the case of the reversal of the direction of segment displacement in Lead II in posterior infarction.

The reason why the intrinsic deflection is sometimes relatively unaffected when positive segment potential change is produced at a cardiac surface, and is sometimes markedly diminished, so that what has been inelegantly called a "high take-off" is produced, was not clearly ascertained in the course of these experiments. In the experiments on obstruction of arterial blood supply, its magnitude seemed to be decreased most when the obstruction was complete. It is therefore probable that, when the deflection in a chest lead which corresponds to the intrinsic deflection in an epicardial lead is markedly decreased in amplitude in comparison with its preintrinsic-like partner, the inference may be drawn that the obstruction is high grade or complete. This statement obviously applies only to the early stages of acute occlusion, before changes in the first part of the QRS complex make their appearance. The sign is of little value in Leads I and III because of interference effects, but, from observations on cases of acute posterior infarction in the early stages, we believe that a marked decrease in the amplitude of

the intrinsic-like deflection in Lead II, with "high take-off," points to high-grade deprivation of arterial blood supply to the area involved.

Although this study did not concern itself with the T wave, we wish to comment on the possible importance of intrinsic and extrinsic, or what, in the case of the RS-T segment, we have called primary and secondary, electrical effects on the form of that deflection. This problem is difficult to study because of the fact that the electrical activity responsible for the T wave is present over all parts of both ventricles at approximately the same time. The importance of subepicardial abnormality in producing changes in the T-wave potential variation at the overlying surface, and consequently in significant body surface leads, is probably just as great as in the case of RS-T segment displacement. So much is easily demonstrable by experiments such as those reported above. Moreover, it has long been known that T-wave changes may be conspicuous in the course of acute pericarditis, in which, presumably, only the subepicardial muscle is involved. It would, however, be of interest to know how secondary effects influence the form of the T wave. Some information on this point can be obtained from a study of left bundle branch block, in which there is so much asynchronism of T-wave deflection of right and left ventricular origin that the summits of the two can be separated. Wolferth and Livezey plan to publish some of the observations on bundle branch block in a subsequent paper, but the following may be said at present: In left bundle branch block, the relatively early, right-ventricular T wave, as recorded in precordial leads with an electrode placed over the right ventricle, has always been upright, in our experience, and tends to be of decidedly greater amplitude than it is when no bundle branch block is present. Over the left ventricle, however, this part of the T wave is always slightly inverted, but the terminal portion of the T wave, which is presumably due to aberrant left ventricular activity, is always upright and of small amplitude. It would appear, therefore, that the large T wave recorded with an exploring electrode over the right ventricle in left bundle branch block is caused by the absence of any effect of secondary potential variation derived from left ventricular activity on the epicardium of the right ventricle, which, under normal circumstances, tends to neutralize, at least to some extent, the primary effect produced locally. The slight inversion of the T wave recorded over the left ventricle, corresponding in time with the large upright T wave over the right ventricle, suggests that secondary right ventricular effects at the surface of the left ventricle are almost negligible. A fragment of evidence with possible bearing on this problem was obtained in the present study. In the normal, the T wave with an exploring electrode in the esophagus at the level of the auricle, or slightly above, is always negative.[28] However, in Fig. 7, it is noted that the T waves obtained with the exploring electrode at those levels were distinctly positive. It is therefore possible that the deformity of the T wave at the epicardial surface caused by digitalis

receives a contribution from the abnormal electrical activity on the endocardial side. The complexity of the subject, however, is such that as yet little can be said about it.

SUMMARY AND CONCLUSIONS

1. RS-T segment displacement recorded with one electrode on a ventricular surface or in a ventricular cavity may be classified as primary or secondary; this is analogous to Lewis' classification of the deflections of the QRS complex as intrinsic and extrinsic. Primary displacement is defined as that which results from abnormal current flow originating in the muscle in close relationship with the exploring electrode, and secondary displacement as that which results from abnormal current flow originating in any other part or parts of the ventricles.

2. The patterns of both primary and secondary displacement vary in certain respects, depending upon the agent used to produce the displacement. This is not in accord with the view that current flow during diastole is solely responsible for RS-T segment displacement recorded during systole, but suggests that, under certain circumstances at least, systolic events play a part.

3. The production of a positive RS-T segment potential change (primary type) at one part of the heart by such diverse means as dilute solutions of potassium chloride, ouabain, or epinephrine, cauterization, trauma, or complete deprivation of blood supply is accompanied by the occurrence of a negative potential change (secondary type) over uninvolved ventricular surfaces.

a. The production of a positive RS-T segment potential change over the entire epicardial surface by solutions of potassium chloride or ouabain causes a corresponding negative potential change within the ventricular cavities.

b. The production of positive RS-T segment potential change over the epicardial surface of the left ventricle causes negative change over the epicardial surface of the right ventricle.

c. The injection of potassium chloride solution toward the endocardial side of the left ventricular wall produces a negative RS-T segment potential change at the overlying epicardial surface, but injection just beneath that surface produces a positive change.

d. Extensive trauma to the endocardial side of the myocardium produces a negative RS-T segment potential change at ventricular epicardial surfaces.

e. Extensive cauterization of ventricular epicardial surfaces produces a positive RS-T segment potential change over the area cauterized and a negative change in other areas. In the one exception recorded, it is possible that an artery supplying a region beyond the area of cauterization had been destroyed. The reversal in direction of potential change at the margin of the area of injury may be abrupt.

f. Complete obstruction of a coronary artery produces a positive RS-T segment potential change at the epicardial surface deprived of its blood supply, and a negative change in other epicardial areas. The reversal in direction occurs at the margin of the area of involvement.

g. Partial obstruction of a coronary artery usually produces either no significant potential change during the RS-T interval at the epicardial surface of the area supplied by that artery, or a positive change, depending upon the grade of obstruction. Moreover, the amplitude of the intrinsic deflection of the QRS complex is affected less by partial, than by complete, obstruction. After cessation of partial obstruction, or even transient complete obstruction, the positive change is converted to negative, and this persists for a short period prior to disappearance of pathologic potential change. For the observation and recording of such events, continuous use of the cardioscope is almost indispensable.

h. In one set of experiments only, of many attempts, using three different methods of producing partial obstruction, was it possible to obtain a negative RS-T segment potential change at the epicardial surface partially deprived of blood supply, without preceding positive change. In this experiment a negative change was also recorded from adjacent areas. An increase in the grade of obstruction produced a positive change over the involved surface.

4. The negative RS-T segment displacement recorded with an exploring electrode over an epicardial region after cessation of obstruction may be of secondary type because of selective involvement of the endocardial side of the myocardial wall.

5. There is as yet no definite evidence that a negative RS-T segment potential change can be produced at a cardiac surface other than as a secondary affect caused by pathologic currents originating elsewhere in the myocardium.

6. A positive or negative RS-T segment displacement recorded by placing an exploring electrode over an anterior or anterolateral epicardial area tends to be associated with a corresponding positive or negative RS-T segment displacement in a chest lead in which the exploring electrode is placed on the surface directly over that epicardial area. It is also highly probable that a positive or negative potential change at a part of the epicardial surface in contact with the diaphragm (during the RS-T interval) is associated with a corresponding positive or negative displacement in Lead II. Judging from the relationships observed in the experiments described above, the patterns of RS-T segment displacement recorded in body surface leads can be accounted for in a much more satisfactory manner than was possible in the past.

7. Although the matter requires much further study, there is already strong evidence to indicate that the direction of RS-T segment displacement recorded with an exploring electrode in the esophagus at the auricular level, or slightly above it, paired with an electrode on an area

of relatively slight potential variation, such as the spine of the right scapula or even the right arm, reflects the direction of potential change in the left endocardial cavity during that interval. In certain cases such a lead may furnish evidence of value as to the location, and possibly also the nature, of myocardial involvement.

8. It is probable that the concept of primary and secondary effects applies to the formation of the T-wave potential change at any cardiac surface area in somewhat the same manner as in the case of RS-T segment potential change, although, under these circumstances, primary and secondary effects coexist. For this reason the demonstration of such relationships, particularly from the quantitative viewpoint, is far more difficult than in the case of the RS-T segment.

REFERENCES

1. Wolferth, C. C., Livezey, M. M., and Wood, F. C.: The Relationships of Lead I, Chest Leads From the C-3, C-4, and C-5 Positions and Certain Leads Made From Each Shoulder Region: The Bearing of These Observations Upon the Einthoven Equilateral Triangle Hypothesis and Upon the Formation of Lead I, AM. HEART J. 21: 215, 1941.
2. Wolferth, C. C., Livezey, M. M., and Wood, F. C.: Studies on the Distribution of Potential Concerned in the Formation of Electrocardiograms, Am. J. M. Sc. 203: 641, 1942.
3. Wolferth, C. C., Livezey, M. M., and Wood, F. C.: Distribution of the Patterns of Ventricular Potential Which Determine the Forms and Significance of Electrocardiograms, Am. J. M. Sc. 205: 469, 1943.
4. Boyd, L. J., and Scherf, D.: The Electrocardiogram After Injury of the Inner Surface of the Heart, Bull. New York Med. College 3: 1, 1940.
5. Burdon-Sanderson, J., and Page, F. J. M.: Experimental Results Relating to the Rhythmical and Excitatory Motions of the Ventricle of the Heart of the Frog and of the Electrical Phenomena Which Accompany Them, Proc. Roy. Soc. 27: 410, 1878; On the Time-Relations in the Excitatory Process in the Ventricle of the Heart of the Frog, J. Physiol. 2: 384, 1879.
6. Bayliss, W. M., and Starling, E. H.: On the Electromotive Phenomena of the Mammalian Heart, Internat. Monats. f. Anat. u. Physiol. 9: 256, 1892.
7. Samojloff, A.: Elektrokardiogrammstudien, Beitr. z. Physiol. u. Path. Festschrift Ludimar Herman, 1908.
8. Eppinger, H., and Rothberger, C. J.: Zur Analyse des Elektrokardiogramms, Wien. klin. Wchnschr. 22: 1091, 1909.
9. Smith, F. M.: The Ligation of Coronary Arteries With Electrocardiographic Study, Arch. Int. Med. 22: 8, 1918.
10. Pardee, H. E. B.: An Electrocardiographic Sign of Coronary Artery Obstruction, Arch. Int. Med. 26: 244, 1920.
11. Parkinson, J., and Bedford, D. E.: Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis), Heart 14: 195, 1927-1929.
12. Barnes, A. R., and Whitten, M. B.: Study of the R-T Interval in Myocardial Infarction, AM. HEART J. 5: 142, 1929.
13. Otto, H. L.: The Ventricular Electrocardiogram. An Experimental Study, Arch. Int. Med. 43: 335, 1929.
14. Wolferth, C. C., and Wood, F. C.: The Electrocardiographic Diagnosis of Coronary Occlusion by the Use of Chest Leads, Am. J. M. Sc. 183: 30, 1932.
15. Wood, F. C., Wolferth, C. C., and Livezey, M. M.: Experimental Coronary Occlusion, Arch. Int. Med. 51: 771, 1933.
16. Wolferth, C. C., and Wood, F. C.: Further Observations Upon the Use of Chest Leads in Electrocardiographic Study of Coronary Occlusion, M. Clin. North America 16: 161, 1932.
17. Wood, F. C., Wolferth, C. C., and Bellet, S.: Infarction of the Lateral Wall of the Left Ventricle: Electrocardiographic Characteristics, AM. HEART J. 16: 387, 1938.

18. Wilson, F. N., MacLeod, A. G., and Barker, P. S.: The Order of Ventricular Excitation in Human Bundle Branch Block, AM. HEART J. 7: 305, 1932.
19. Wilson, F. N., MacLeod, A. G., Johnston, F. D., and Hill, I. G. W.: Monophasic Electrical Response Produced by the Contraction of Injured Heart Muscle, Proc. Soc. Exper. Biol. & Med. 30: 797, 1933.
20. Bellet, S., and Johnston, C. G.: The Effect of Coronary Occlusion Upon the Initial Phase of the Ventricular Complex in Precordial Leads, J. Clin. Investigation 13: 725, 1934.
21. Thompson, W. P.: The Electrocardiogram in the Hyperventilation Syndrome, AM. HEART J. 25: 372, 1943.
22. Master, A. M.: The Electrocardiogram and X-ray Configuration of the Heart, Philadelphia, 1942, Lea and Febiger, p. 364.
23. Barnes, A. R., and Mann, F. C.: Electrocardiographic Changes Following Ligation of the Coronary Arteries of the Dog, AM. HEART J. 7: 477, 1931.
24. Osterhout, W. J. V.: The Nature of the Action Current in Nitella, J. Gen. Physiol. 27: 61, 1943; A Model of the Potassium Effect, J. Gen. Physiol. 27: 91, 1943.
25. a. Lewis, T., Meakins, J., and White, P. D.: The Excitatory Process in the Dog's Heart. Part I. The Auricles, Philosophical Transactions, Roy. Soc. of London, series B, 205: 375, 1914; b. Lewis, T., and Rothschild, M. A: Part II. The Ventricles, ibid. 206: 181, 1915.
26. Brown, W. H.: Study of Esophageal Lead in Electrocardiography, AM. HEART J. 12: 1, 1936; 12: 307, 1936.
27. Dearing, W. H., Barnes, A. R., and Essex, H. E.: Experiments With Calculated Therapeutic and Toxic Doses of Digitalis. II. Effects on the Electrocardiogram, AM. HEART J. 25: 665, 1943; I. Effects on the Myocardial Cellular Structure, AM. HEART J. 25: 648, 1943; VI. Comparative Effects of Toxic Doses of Digitalis and of Prolonged Deprivation of Oxygen on the Electrocardiogram, Heart and Brain, AM. HEART J. 27: 108, 1944.
28. Helm, J. D., Jr., Helm, G. H., and Wolferth, C. C.: The Distribution of Potential of Ventricular Origin Below the Diaphragm and in the Esophagus, AM. HEART J. 27: 755, 1944.

THE TREATMENT OF ORTHOSTATIC HYPOTENSION

With Particular Reference to the Use of Desoxycorticosterone

Raymond Gregory, M.D.
Galveston, Texas

BRADBURY and Eggleston[1] described a syndrome which they designated "postural hypotension." This syndrome consists of marked weakness, dizziness, normal blood pressure in the sitting or reclining positions, marked fall in blood pressure in the upright position, an insignificant elevation in the cardiac rate in the upright position, impairment of sweating, and accentuation of symptoms in hot weather. They thought that these symptoms indicated a defect in the function of the sympathetic nervous system. This concept has continued to dominate discussions concerning the etiology, as shown by the report of Ellis and Haynes,[2] who emphasized the relationship between orthostatic hypotension* and disease of the nervous system. Jeffers, Montgomery, and Burton,[3] Stead and Ebert,[4] Freeman and Robertson,[5] and Laufer[6] have confirmed these observations and interpretations, and have furthered the concept that the syndrome is due to inadequate vasomotor function. It has been demonstrated repeatedly, however, that this abnormality may occur in cases in which no disease of the nervous system can be discovered by clinical means.

Although defects in the reflex sympathetic vasomotor control and increase in the cardiac rate in the upright position have been thought generally to be the most important factors in the pathogenesis of this abnormality, MacLean and Allen[7] and MacLean, Allen, and Magath[8] have suggested and presented evidence that the fault lies in failure to maintain adequate return of venous blood to the heart. Hallock and Evans[9] have shown that there are a decrease in blood volume and hemoconcentration in this disease when the patient is in the upright posture, and they have suggested that abnormal filtration rates aggravate the circulatory embarrassment. Hallock and Evans have also observed, as have others, including myself, that this condition may be associated with orthostatic tachycardia.

The treatment of orthostatic hypotension has consisted of various mechanical procedures, such as tight abdominal and leg binders, the "head-up" sleeping position described by MacLean and Allen,[7] the

From the Department of Internal Medicine, University of Texas School of Medicine, Galveston, Texas.

Received for publication June 2, 1944.

*The desoxycorticosterone used in this study was "Cortate," Schering Corporation brand of synthetic desoxycorticosterone in sesame oil. Generous amounts of the substance were supplied by Dr. W. R. Bond, Medical Research Division, Schering Corporation, Bloomfield, N. J.

The paredrine, paredrinol, and neosynephrin were made available by the generosity of Frederick B. Stearns Company, Detroit, Dr. Richard Johnson, Medical Director.

avoidance of any type of strenuous exertion on warm days, and the use of various vasoconstrictor drugs such as have been described by Jeffers, Montgomery, and Burton,[3] Davis and Davis,[10] Korns and Randall,[11] Stead and Ebert,[4] and others.

A patient who presented most of the classical manifestations of orthostatic hypotension has been studied. The effects of the "head-up" sleeping position and of ephedrine, benzedrine, paredrine, paredrinol, neosynephrin, and epinephrine in oil have been observed. With the exceptions to be noted, the procedures and agents proved unsatisfactory.

It was therefore decided to utilize the well-established capacity of desoxycorticosterone to increase blood volume as a method of maintaining an adequate blood pressure in the upright position. The benefits to the patient have been so marked that our observations with this drug form the principal basis for this report.

CASE REPORT

A white woman, aged 48 years, complained of poor health since a pelvic operation eighteen years earlier, and said that her symptoms had been worse since a pregnancy eleven years earlier. Her principal symptoms during all these years had been weakness, increasing dizziness, and a dry skin. For three to four years she had fainted frequently upon assuming the upright position. This was particularly true upon arising and for the remainder of the early morning. Her life for eighteen months to two years before she was seen had been spent primarily in running in a crouched position from one chair to another to avoid extreme dizziness and fainting. In the sitting or recumbent position she was entirely free of the above complaints.

A thorough physical examination was essentially negative, with exceptions to be noted. Subsequently, many attempts were made to discover disease of the nervous system, but no abnormality was discovered. Hypersensitive carotid sinus reflexes of any of the three types were considered and discarded because of inability to reproduce any of her symptoms by vigorous massage over both carotid sinuses. Addison's disease was ruled out because of lack of increased pigmentation, no crises during her years of complaint, and normal blood sugar, sodium, potassium, and chloride values.

The blood pressure was 130/85 with the patient in the recumbent position, and when she assumed the upright position it fell to 80/50; it immediately returned to previous levels upon lying down. After a few minutes in the upright position the blood pressure fell to 50/?, and dizziness was marked. These observations were confirmed on numerous occasions. Not infrequently the systolic blood pressure would fall to 40 mm. Hg, or lower, and she would faint. The cardiac rate sometimes rose to 100 or 110 beats per minute when the patient was in the upright position.

A diagnosis of orthostatic hypotension was made, and attempts at therapy were begun along conventional lines.

TREATMENT

The patient was required to sleep in the "head-up" position for a number of weeks, as recommended by MacLean and Allen, but she insisted that no benefit was derived. Unfortunately, no blood pressure

readings were made during that period. Benzedrine and ephedrine were used for a few days, but it was necessary to discontinue them because of the resulting nervousness and insomnia.

Paredrine hydrobromide by mouth was then tried, with considerable benefit for a while. In time, however, she appeared to develop tolerance, which required increasing the dose and shortening the interval between doses. Finally she was convinced that it gave her no benefit. Paredrinol was given, but there was inadequate objective evidence of any improvement in one trial. Detailed data of our experience with these two drugs are shown in Tables I and II.

TABLE I

EFFECT OF PAREDRINE HYDROBROMIDE

DATE	DRUG	DOSE (MG.)	TIME	BLOOD PRESSURE		VERTIGO OR FAINTNESS	REMARKS
				LYING	STANDING		
3/ 9/43	Paredrine hydrobromide	40	7:00 A.M.				
		20	9:30 A.M.				
		20	12:30 P.M.				
			1:30 P.M.	115/75	60/30(?)	Slight faintness	
			1:40 P.M.	115/75	55/40	Moderate faintness	
	Paredrine hydrobromide	80	1:45 P.M.				
			2:20 P.M.	145/85	110/75		
			2:22 P.M.		110/75		
			2:29 P.M.		120/80		
			2:35 P.M.		110/75		
			4:00 P.M.		110/75		
			4:20 P.M.				Walked to another room
			5:00 P.M.	135/120	60/45	Marked dizziness	
	Paredrine hydrobromide	60	½ hr. before arising				Able to be up better
		40	q. 2 h.				
3/30/43	Paredrine hydrobromide	40	7:45 A.M.				No insomnia
		40	9:45 A.M.				
		40	11:45 A.M.				
			1:30 P.M.	140/85	65/50		
	Paredrine hydrobromide	40	1:45 P.M.				
			2:00 P.M.	135/85	70/50		
			2:30 P.M.		80/50		
			2:35 P.M.	110/80 (sitting)	90/70		
			3:18 P.M.		90/65		
4/ 5/43	Paredrine hydrobromide	80	2:00 P.M.				
			4:45 P.M.	110/80	65/50		
	Paredrine hydrobromide	80	4:46 P.M.				Itching and burning of skin
			5:25 P.M.	128/85	90/70		
			5:35 P.M.		90/60		

Neosynephrin hydrochloride was used next. This drug produced the greatest benefit of any of the vasoconstrictors used. It was impossible to continue to obtain the drug in sufficiently large doses (50 mg.), and it was discontinued because taking five to seven capsules of 10 mg. each

TABLE II

EFFECT OF PAREDRINOL AND PAREDRINE

DATE	DRUG	DOSE (MG.)	TIME (P.M.)	BLOOD PRESSURE		DIZZINESS OR FAINTNESS	REMARKS
				LYING	STANDING		
5/11/43	None			90/60	45/? to 0		Fainted
	Paredrinol	60	1:45				
			2:20	85/60			
			2:55	100/70			
			2:59	35-40/?	sitting		Faint
	Paredrine	60	3:00				
			3:55	100/70			
			3:57		50/?		
			5:20	140/90	75/55		

TABLE III

EFFECT OF NEOSYNEPHRIN HYDROCHLORIDE

DATE	DRUG	DOSE (MG.)	TIME (P.M.)	BLOOD PRESSURE		DIZZINESS OR FAINTNESS	REMARKS
				LYING	STANDING		
6/29/43	None		1:33	110/70	50/?	Very dizzy	
	Neosynephrin hydrochloride	50	1:37				
			2:55	140/92	100/70	No symptoms	
			2:58		85/60	No symptoms	Walked down hall
			3:00		90/60		
			3:02		90/60		
	Neosynephrin hydrochloride	50	3:03				
			4:00	145/90			
			4:01		110/80		
			4:03		92/65		
			4:05		70/55		
			4:07		70/55	No symptoms	Feels fine Unable to continue to get 50 mg. capsules

TABLE IV

EFFECT OF EPINEPHRINE IN OIL

DATE	DRUG	DOSE (C.C.)	TIME (P.M.)	BLOOD PRESSURE		SYMPTOMS	REMARKS
				LYING	STANDING		
10/1/43	Epinephrine in oil I. M.	0.4	1:58				
			2:03	105/70	55/40	Dizzy	
			2:51	160/90	100/60		
			2:53		80/55		
			2:54		80/55		
			2:56		70/50		Walking around
			3:02		105/70		Walking
			3:07		100/70		Walking
			3:08		100/68		Standing
			4:50		70/55	No symptoms	
			4:56		65/45		Rubbed arm 2 min.
			4:58			Palpitation	
			5:00		120/80		
			5:02		120/80		No symptom since original dose

at intervals of one to two hours made the patient nauseated. Detailed observations are given in Table III. I consider that neosynephrin hydrochloride was beneficial to this patient. It will be noted from the data in Table III that the effects were beginning to decrease markedly in one hour. The dose had to be repeated at no greater than two-hour intervals.

TABLE V. EFFECT OF DESOXYCORTICOSTERONE ACETATE

DATE	DRUG	DOSE (MG.)	TIME	BLOOD PRESSURE		SYMPTOMS	REMARKS
				LYING	STANDING		
2/14/44	None		2:17 P.M.	120/90	50/?	Weak and faint	
	DOCS*	10	2:23 P.M.				Felt much improved in 2 hr. for rest of evening
2/15/44	DOCS	10		142/100†	55/?		
2/16/44	DOCS	10					
			3:37 P.M.	152/102			
			3:38 P.M.		105/75		
			3:40 P.M.		95/70		
			3:52 P.M.		80/55		
	DOCS	10	3:53 P.M.				
2/17/44							Felt better than for years, walked across street and back
			2:49 P.M.	156/105	90/60		
	DOCS	5	3:07 P.M.				NaCl 1 Gm.
2/19/44			2:15 P.M.	130/ 88	55/40		
	DOCS	10	2:20 P.M.				NaCl 2 Gm.
2/20/44			11:30 A.M.	150/100	110/75		Noted beneficial effects in 1 hour
	DOCS	10	11:50 A.M.				NaCl 2 Gm.
2/21/44			2:30 P.M.	160/105	120/80		Went shopping (first time in 2 years)
	DOCS	5	2:50 P.M.				NaCl 5 Gm.
2/22/44	DOCS	5		150/ 90	82/60		NaCl 10 Gm.
2/23/44	DOCS	5		155/ 98	130/80		NaCl 10 Gm.
2/24/44	DOCS	5		154/100	130/84		NaCl 15 Gm.
2/25/44	DOCS	5		165/105	120/80		NaCl 15 Gm.
2/26/44	None			165/110	110/80	Severe headache sitting or lying	
2/27/44	None			166/110	110/82		NaCl 15 Gm.
2/28/44	None				110/80		NaCl 15 Gm.
4/15/44	DOCS	5	q. 5 to 7 days	125/80†	100/70	None	NaCl 15 Gm.
4/20/44	DOCS	5	1:40 P.M.	122/82†			
			1:41 P.M.		90/66		
			1:46 P.M.		80/64		Continued standing
4/25/44	DOCS	5	1:30 P.M.	142/100†			
			1:31 P.M.		90/70		NaCl 20 Gm.
			1:37 P.M.		76/58		Continued standing

*DOCS = desoxycorticosterone acetate.
†Sitting.

TABLE V—CONT'D

DATE	DRUG	DOSE (MG.)	TIME	BLOOD PRESSURE		SYMPTOMS	REMARKS
				LYING	STANDING		
4/29/44	DOCS	5	3:30 P.M.	145/102†			NaCl 20 Gm.
			3:31 P.M.	154/102†			NaCl 20 Gm.
			3:31 P.M.				Stood up
			3:32 P.M.		105/84		NaCl 20 Gm.
			3:33 P.M.		100/84		Started walking
			3:37 P.M.		94/70		Continued walking
5/ 4/44	DOCS	5					NaCl 20 Gm.
5/ 9/44	DOCS	5					NaCl 20 Gm.
5/13/44	DOCS	5	4:22 P.M.	142/100† (5 min.)			Stood up
			4:22½ P.M.		120/88		NaCl 20 Gm.
			4:24 P.M.		112/90		Started walking
			4:27 P.M.		95/68		NaCl 20 Gm.

No central nervous system symptoms were ever observed. It is unfortunate that it was not commercially available in dosage units adequate for the treatment of orthostatic hypotension.

Epinephrine in oil proved to be of definite benefit to this patient, as shown by the detailed observations in Table IV. The injection was given in the arm. The data show that the effects began to decrease within one hour after injection. Walking, however, increased the blood pressure of the patient in the upright position. It may also be noted that vigorous massage of the injection site produced further beneficial effect as long as three hours after the injection.

Epinephrine in oil was continued for two months with benefit. It became necessary to discontinue it because of extreme tissue reactions at the site of injection. I believe from this limited experience that epinephrine in oil deserves further consideration in the treatment of orthostatic hypotension.

The capacity of desoxycorticosterone to increase the blood volume was considered. It was thought that the blood volume could be safely raised by this method far enough to prevent the fall of the blood pressure to levels which would produce symptoms. Our experience with this drug has been most gratifying. The patient has returned to all the usual activities of her life for the first time in many years.

Desoxycorticosterone acetate in oil was injected intramuscularly in conjunction with sodium chloride by mouth. In addition to its complete effectiveness, it has the further comparative advantage that it need be administered only every five to seven days, whereas the vasoconstrictor drugs must be taken every one to three hours daily. The detailed data are presented in Table V.

The possible dangers of desoxycorticosterone must be emphasized. These dangers have been reported repeatedly. It is essential that this very potent substance be employed with rigid control of the blood pressure and weight. This is particularly essential when desoxycorticosterone is employed in conjunction with added sodium chloride, as we have done, to reduce the dosage of desoxycorticosterone to a minimum.

It will be noted from the data in Table V that severe and persistent headaches occurred as a result of the elevated blood pressure during the period in which the dosage level was being established.

As a general rule, the patient felt much stronger in the afternoons. Believing this morning weakness might be due to failure to take sodium

chloride for about twelve hours, another 5 Gm. of sodium chloride were added, and the total of 20 Gm. were divided equally through the twenty-four hours. Since the institution of this regime of salt, she feels much stronger in the mornings than had been the case previously.

It has been demonstrated on frequent occasions, as can be seen from the data in Table V, that the administration of salt alone is inadequate to maintain the blood pressure at normal levels in the upright position. This is significant in view of the claims of MacLean, Allen, and Magath[8] that added salt was of value in the management of orthostatic hypotension.

Subcutaneous implantation of pellets of desoxycorticosterone according to the method of Thorn[12] has been considered. The patient has hesitated because of the simplicity of the present management.

SUMMARY AND CONCLUSIONS

A case of orthostatic hypotension is reported, and detailed objective evidence of the value of various therapeutic agents is presented and briefly discussed.

Attention is called particularly to the therapeutic value of small doses of desoxycorticosterone acetate in oil by intramuscular injection, in conjunction with an increased oral intake of sodium chloride in orthostatic hypotension.

REFERENCES

1. Bradbury, S., and Eggleston, C.: Postural Hypotension, Am. Heart J. 1: 73, 1925.
2. Ellis, L. B., and Haynes, F. W.: Postural Hypotension, Arch. Int. Med. 58: 773, 1936.
3. Jeffers, W. A., Montgomery, H., and Burton, A. C.: Types of Orthostatic Hypotension and Their Treatment, Am. J. M. Sc. 202: 1, 1941.
4. Stead, E. A., and Ebert, R. V.: Postural Hypotension. A Disease of the Sympathetic Nervous System, Arch. Int. Med. 67: 546, 1941.
5. Freeman, H. E., and Robertson, J. E.: Orthostatic Hypotension Accompanying the Tabetic Form of Dementia Paralytica, Arch. Dermat. & Syph. 46: 796, 1942.
6. Laufer, S. T.: Orthostatic Hypotension, Canad. M. A. J. 46: 160, 1942.
7. MacLean, A. R., and Allen, E. V.: Orthostatic Hypotension and Orthostatic Tachycardia, J. A. M. A. 115: 2162, 1940.
8. MacLean, A. R., Allen, E. V., and Magath, T. B.: Orthostatic Tachycardia and Orthostatic Hypotension: Defects in the Return of Venous Blood to the Heart, Am. Heart J. 27: 145, 1944.
9. Hallock, Phillip, and Evans, Gerald: Effect of Posture on Circulating Blood Volume in a Case of Orthostatic Hypotension and Tachycardia, Proc. Soc. Exper. Biol. & Med. 47: 460, 1941.
10. Davis, P. L., and Davis, M. S.: Orthostatic Hypotension. The Treatment of Two Cases With Benzedrine Sulfate, J. A. M. A. 108: 1247, 1938.
11. Korns, H. M., and Randall, W. L.: Benzedrine and Paredrine in the Treatment of Orthostatic Hypotension, With Supplementary Case Report, Ann. Int. Med. 12: 253, 1938.
12. Thorn, G. W.: Clinical Use of Extracts From Adrenal Cortex, J. A. M. A. 125: 10, 1944.

ADDENDUM

This patient has been taking desoxycorticosterone for slightly more than a year. For many months, 5 mg. of desoxycorticosterone, plus 15 to 20 Gm. of salt daily, continued to give her satisfactory relief with the exception of the early morning hours. For this reason, three pellets of Percorten, 125 mg. each, were implanted cautiously at about three-to four-week intervals. Since the implantation of these pellets it has been possible for this patient to get along on an injection schedule of 5 mg. twice weekly. We have found this schedule the most satisfactory one that we have tried up to the present time.

Clinical Reports

HEMOCHROMATOSIS WITH COMPLETE HEART BLOCK

With a Discussion of the Cardiac Complications

Donald W. Petit, M.D.
San Francisco, Calif.

ALTHOUGH a huge literature on hemochromatosis has accumulated since Trousseau's[1] description little has been said in the American and English writings on the cardiac complications of this disease. Our interest in the subject was aroused by the following case.

CASE REPORT

A. Mc. (S.U.H. 216076), aged 35 years, entered the hospital Oct. 16, 1942, complaining of fatigability, weakness, impotence, loss of libido, and pigmentation of the skin for the preceding two or three years. His past history was not remarkable; there was no story suggestive of rheumatic fever, syphilis, or chronic alcoholism. His present illness consisted of a group of signs and symptoms which he thought began after an attack of "flu" in February, 1940; after this he began to notice that he tired easily, that normal libido was absent, and that in the succeeding year his skin gradually became darker; he thought there had been some loss of hair from the arms and legs. By the summer of 1941 he felt better except for impotence and fatigue. In November, 1941, and again in January, 1942, he had two ten-day febrile periods, with fever to 105° F. The nature of these attacks was not clear. As a sequel to each, there was an increase in general weakness and malaise. In addition, he said that his heart rate fell from 60 to 34 in January, 1942, and that it had never been faster thereafter. Both of the febrile illnesses were treated with sulfonamides. He made a partial recovery, but, in the spring of 1942, noticed that he was short of breath on exertion and that he had occasional precordial pains which were not made worse by exertion. In July, 1942, on a mountain trip (elevation 11,500 feet), he became acutely ill, with severe dyspnea, marked weakness, and massive swelling of the legs and abdomen. Rest in bed and diuretics brought about a remission of symptoms. However, he felt weak ever after, and his weight declined from 170 to 135 pounds. About three weeks prior to entry he noticed frequency of urination and excessive thirst; on Oct. 7, 1942, he was admitted to the Santa Monica Hospital "in diabetic coma with hyperglycemia, glycosuria and ketonuria"; his diabetes was controlled fairly easily, and he was put on a maintenance dose of 10 units of regular insulin, morning and evening. Examinations of the urine at that hospital were

From the Department of Medicine, Stanford University School of Medicine, San Francisco.
Received for publication Oct. 1, 1943.

reported as "positive for hemosiderin crystals." He was sent to San Francisco, and entered Stanford Hospital Oct. 16, 1942.

Physical Examination.—He was a thin young man, with a slaty, gray, dirty, diffuse pigmentation of the skin, most prominent on the backs of the hands, on the face, and in the skin creases. There was no obvious pigmentation of the mucous membranes. The distribution of hair was feminine in type. Examination of the eyes, ears, nose, and throat showed nothing remarkable. A few moist râles could be heard in the right lung. The heart was enlarged to the left; the heartbeat was regular, with a rate of 44. In early diastole an extra sound, such as might be associated with auricular systole, was heard. The sounds otherwise were not remarkable. The blood pressure was 110/80. The abdomen was moderately distended, with signs of ascites. The liver was firm and slightly tender, and extended below the umbilicus. The spleen was not palpable. There were no obvious penile or testicular abnormalities. The legs and thighs were the seat of massive, soft, pitting edema. Neurological examination showed nothing remarkable.

Laboratory Data.—The erythrocyte count was 3.63 million per cubic millimeter, with a hemoglobin content of 13.5 Gm. (75 per cent Sahli); the leucocyte count was 8,400 per cubic millimeter. The blood Wassermann and Hinton reactions were negative. The urine was normal. The fasting blood sugar was 256 mg. per cent. The blood urea on entry was 42 mg. per cent, and the plasma chlorides were 544 mg. per cent (as sodium chloride). The direct van den Bergh was negative; the indirect was 2.4 units, with an icterus index of 19. The serum proteins (Kagan falling drop method) were 5.7 grams. A bromsulfalein dye excretion test (2 mg. per kilogram) showed 10 per cent retention of the dye in the serum after thirty minutes. The venous pressure (five days after entry) was 18 cm. of saline solution as measured in the antecubital fossa; the arm-to-tongue circulation time (with 20 per cent Decholin) was sixty seconds. The vital capacity was 3.3 liters.

Roentgenologic examination of the abdomen and skull revealed no abnormalities. A roentgenogram of the chest on Oct. 16, 1942, showed marked enlargement of the heart (Fig. 1). Electrocardiograms taken from Oct. 19, 1942, until Nov. 3, 1942, showed complete auriculoventricular block, with low voltage ventricular complexes, abnormal T waves, and right axis deviation (Fig. 2).

A skin biopsy showed marked deposition of iron around the sweat glands.

The diagnosis of hemochromatosis was made, although it was thought that this did not explain everything; the possibility that the ascites and massive edema were secondary to cirrhosis of the liver was entertained, but, because of the cardiac abnormalities, the likelihood of heart failure was considered more probable. The hyperglycemia was of the sort usually seen in hemochromatosis, and will be dismissed here with the statement that his diabetes was adequately controlled with a diet of 270 Gm. of carbohydrate, 90 Gm. of protein, 60 Gm. of fat, and 40 units of protamine zinc insulin daily.

Digitalis was administered with an initial dose of 0.6 Gm., then 0.4 Gm. on the following day, 0.2 Gm. daily for the next six days, and 0.1 Gm. daily, thereafter. He was given 0.5 c.c of mercupurin, and 1.5 c.c. two days later. There was prompt and impressive diuresis, with a weight loss from 70.5 kilograms to 57.1 kilograms in six days.

Along with this there was complete disappearance of the edema and ascites. The liver became much smaller, as did the heart (Fig. 3). The venous pressure fell to 5 cm. of saline solution, and the arm-to-tongue circulation time to 21 seconds; the arm-to-lung circulation time (done with ether) was 16 seconds. The direct van den Bergh was negative; the indirect was 0.68 units; the icterus index was 6 (Nov. 3, 1942). The electrocardiographic studies were interesting, in that, with the administration of digitalis, the auricular rate fell from 103 to 71, whereas the ventricular rate fell slightly, from 44 to 36.

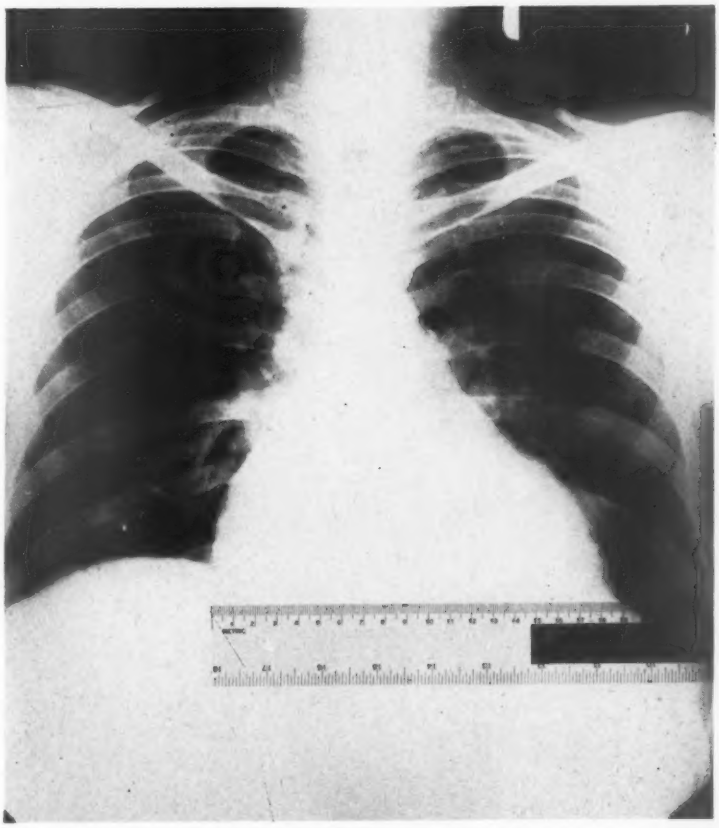


Fig. 1.—Roentgenogram of the heart before treatment.

The patient was dismissed on Nov. 7, 1942; he was in fair condition, was taking digitalis in a dose of 0.1 Gm. daily, and had no signs of heart failure. In January, 1943, word was received that he had died. Dr. J. P. Sampson, his personal physician, and Dr. A. A. Kosky sent some pieces of tissue to the Department of Pathology for study. There were no gross abnormalities of the heart valves or coronary vessels. Examination of the sections showed, in general, the characteristic changes of hemochromatosis, with iron deposition in the heart, liver, adrenals, pancreas, and, to a less extent, in the kidneys and lungs. Of special interest were the heart specimens. These showed localized areas of atrophy in the myocardium. The muscle fibers contained

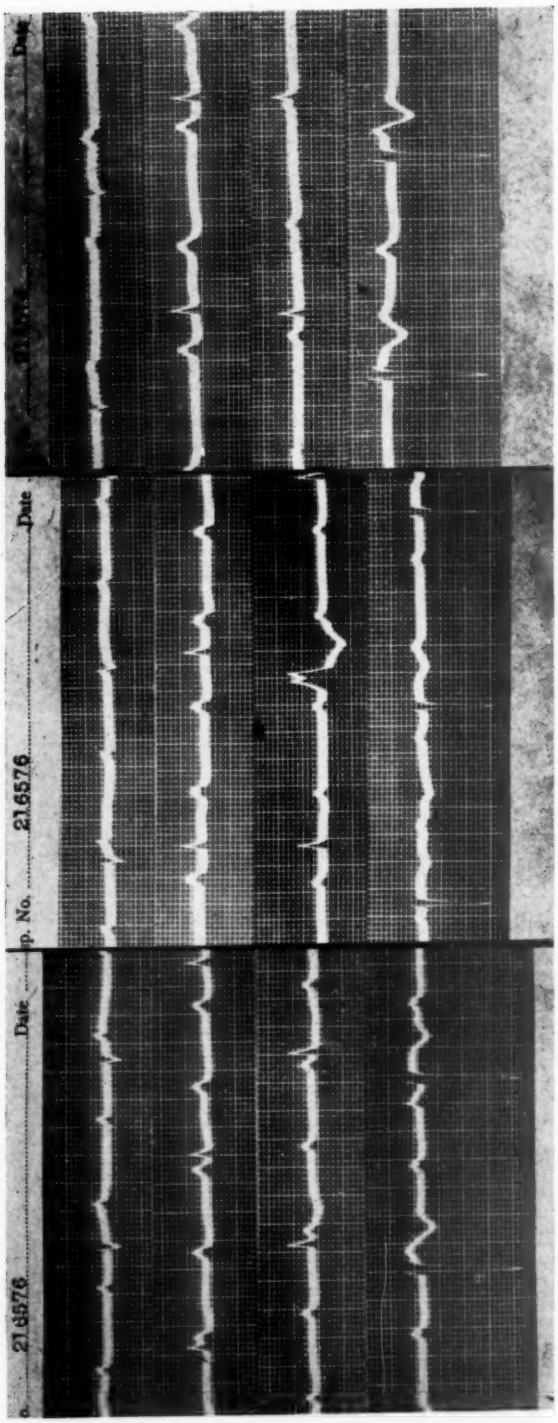


Fig. 2.—Electrocardiograms on October 19, October 24, and November 3.

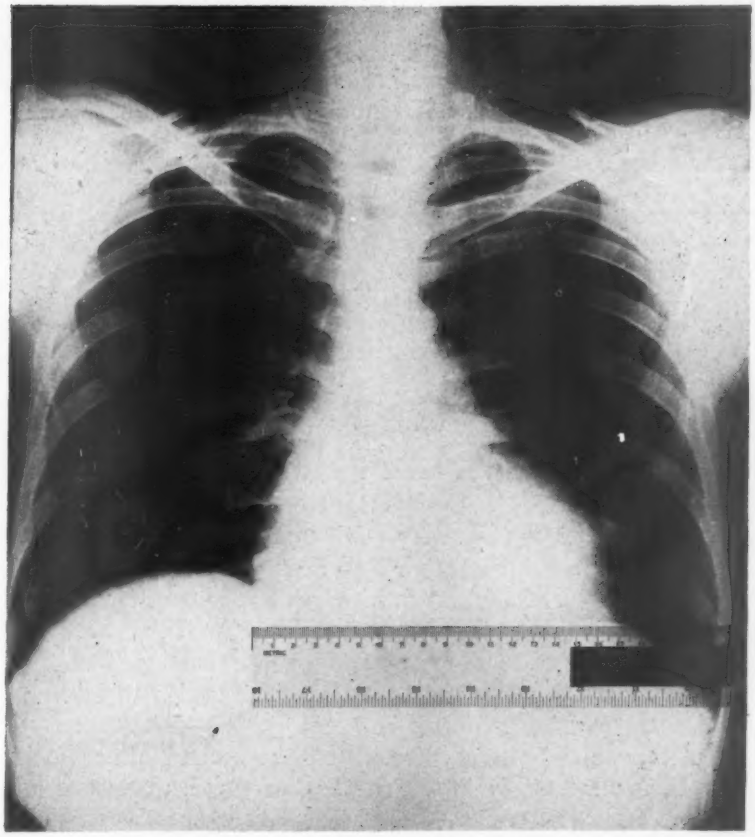


Fig. 3.—Roentgenogram of the heart after treatment.

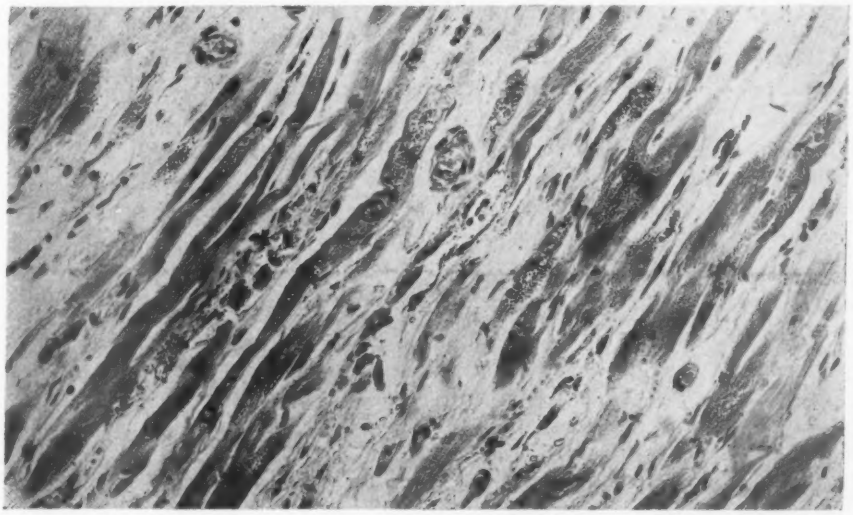


Fig. 4.—Microscopic sections of the heart muscle, showing pigmented granules in the fibers.

dark brown pigment granules, and special stains showed numerous fat droplets. There was considerable variation in the size of the individual fibers; some terminated in threadlike processes. There were numerous broad spaces between fibers, containing fibroblasts and pigment-filled macrophages (Fig. 4). It was the opinion of Dr. Cox and his associates in the Department of Pathology that these changes could be interpreted as evidence of injury to the heart. The sections did not contain the bundle of His, so that the exact anatomic cause of the heart block is not known.

In reviewing the histories of about a dozen cases of hemochromatosis which have been seen at Stanford Hospital, none was similar to the one described here. In cases with autopsy reports there was no mention of myocardial fibrosis, although the sections in some showed as much iron as did this patient's heart.

DISCUSSION

This patient presented the usual features of hemochromatosis, plus heart failure with complete auriculoventricular block. In a search for data on the cardiac complications of hemochromatosis, the standard English textbooks on heart disease were examined, but no pertinent reference was found. Sheldon,[2] in his thorough monograph, makes the statement that "several cases have died from heart failure," but has little further comment. Only four[3-6] adequate reports on heart failure and hemochromatosis could be found in the English literature, and, of these, only two[3, 4] emphasize the heart failure. The first of these[3] concerned a man, 54 years of age, and the second[4] described three cases of hemochromatosis in which the heart was abnormal. These patients were men, aged 59, 43, and 21 years, respectively. The last case was comparable to ours, for not only was heart failure present, but it was associated with complete auriculoventricular block, and at one time with auricular flutter.

In contrast to the few English reports, there is a large French literature on cardiac disorders in hemochromatosis.[7-19] The authors describe fully some twenty cases of heart failure in young adults with "bronzed diabetes." The most complete discussion is that of R. de Vēricourt.[19] It is the opinion of the French that there is a symptom complex, "syndrome endocrino-hepato-cardiaque," in which there are all of the common manifestations of hemochromatosis, plus heart failure; this occurs almost exclusively in young adults. The French authors discuss this syndrome in great detail, and seem familiar with it as an entity.

Counting the four cases in the English literature, twenty-five case reports were reviewed. All but three of the patients were under 45 years of age; of the three, two were 54 years old and one was 59 years old. There were two cases[5, 17] in women, aged 34 and 18 years, respectively. Cardiac arrhythmias were not uncommon. There were two cases[4, 5] with auricular fibrillation, one with auricular tachycardia[5] and, interestingly enough, two besides our own with complete auriculo-

ventricular block.[4, 10] The remainder apparently had regular sinus rhythm, although, in two,[6, 12] frequent premature beats were noted. In three cases[9, 10, 12] "low voltage" in the electrocardiogram was reported. Two patients[5, 6] complained of severe, tearing, chest pain. Subsequent autopsy revealed no coronary artery disease or evidence of infarction in either case. The response to therapy could not be predicted from a study of the cases. Some patients[14] failed to improve whereas others improved markedly, only to fail again shortly. One patient[10] was followed for seven years. The average duration of life after the development of heart failure was about nine months. The cause of these cardiac complications is not known. The French writers are convinced that they are not the result of local damage to the heart by iron. They emphasize the lack of fibrosis and absence of derangement of myocardial architecture in the cases they studied histologically. They attribute the heart failure to some generalized metabolic disorder whose nature is uncertain. On the other hand, Blumer and Nesbit[3] and Maling and Riley[6] demonstrated extensive fibrosis in the heart muscle in their cases. Kerr and Althausen[4] apparently feel that local damage to the heart is important, for they speculate upon the possibility that heart failure may be seen more frequently in hemochromatosis since the patients are enabled to live longer by the use of insulin.

In our own case the heart muscle did show some signs of injury that could have played a part in the production of heart failure. The presence of auriculoventricular block is evidence of local tissue damage. Unfortunately, there are no adequate series of cases of hemochromatosis with and without heart failure which would enable one to correlate clinical data with anatomic observations. Sheldon[2] and Butt and Wilder[20] describe heavy iron pigmentation of the heart muscle, but there is no mention of fibrosis or scarring.

CONCLUSIONS

A case of hemochromatosis with heart failure and complete heart block is described.

The importance of the cardiac complications, which are emphasized in the French literature, has not been sufficiently stressed in the English writings on hemochromatosis.

The mechanism of the production of cardiac failure and disturbances of rhythm in hemochromatosis is discussed.

REFERENCES

1. Trousseau, A.: Clinical Medicine, 1868-1872, New Sydenham Society, vol. III, pp. 500-502.
2. Sheldon, J. H.: Haematochromatosis, London, 1935, Oxford University Press.
3. Blumer, G., and Nesbit, R. R.: Case of Hemochromatosis with Degeneration of Heart Muscle and Death From Congestive Heart Failure, New England J. Med. **218**: 295, 1938.

4. Kerr, W. J., and Althausen, T. L.: Hemochromatosis. Report of Three Cases With Endocrine Disturbances and Notes on Previously Reported Case. Discussion of Etiology, Endocrinology 17: 621, 1933.
5. Murray Lyon, R. M.: Haemochromatosis: Report on 3 Cases, Brit. M. J. 1: 1297, 1936.
6. Maling, T. C., and Riley, G.: Haemochromatosis: Report on Case, New Zealand M. J. 36: 314, 1937.
7. Bezancon, F., de Gennes, L., Delarue, J., and Oumansky, V.: Cirrhose pigmentaire avec infantilisme, insuffisance cardiaque et aplasies endocriniennes multiples, Bull. et mém. Soc. méd. d. hôp. de Paris 48: 967, 1932.
8. Bouchut, L., Levrat, M., Froment, R., and Loras, O.: Les complications cardiaques des cirrhoses pigmentaires. Myocardite pigmentaire? J. de méd. de Lyon 16: 611, 1935.
9. Clerc, A., Bascourret, M., and Andrè, R.: Cirrhose pigmentaire avec atrophie testiculaire et insuffisance grave du cœur, Bull. et mém. Soc. méd. d. hôp. de Paris 51: 1228, 1935.
10. Donzelot, E.: L'insuffisance cardiaque bronzée, Arch. d. mal. du cœur 29: 1, 1936.
11. Donzelot, E., and de Vēricourt, E. R.: Un cas d'insuffisance cardiaque bronzée; syndrome endocrino-hépato-myocardique, Arch. d. mal. du cœur 31: 226, 1938.
12. de Gennes, L., Delarue, J., and de Vēricourt, R.: Sur un nouveau cas de cirrhose pigmentaire avec infantilisme et myocardie. Le syndrome endocrino-hépato-cardiaque, Bull. et mém. Soc. méd. d. hôp. de Paris 51: 1088, 1935.
13. de Gennes, L., Delarue, J., and de Vēricourt, R.: Le syndrome endocrino-hepáto-cardiaque (étude des cirrhoses pigmentaires avec infantilisme et myocardie), Presse méd. 44: 377, 1936.
14. de Gennes, L., and Germain, A.: Sur deux nouveaux cas de cirrhose pigmentaire avec infantilisme et defaillance cardiaque (syndrome endocrino-hépato-cardiaque), Bull. et mém. Soc. méd. d. hôp. de Paris 56: 665, 1940.
15. Germain, A., and Morvan, A.: Cirrhose bronzée avec infantilisme et insuffisance cardiaque, Bull. et mém. Soc. méd. d. hôp. de Paris 53: 157, 1937.
16. Labbē, M., Boulin, R., Uhry, P., and Bour, H.: Diabete bronzée avec infantilisme et insuffisance cardiaque, Bull. et mém. Soc. méd. d. hôp. de Paris 52: 515, 1936.
17. Oumansky, V., and Longuet, A.: Le Syndrome endocrino-cardiaque, Presse méd. 46: 388, 1938.
18. Waldorp, C. P., Genijovich, S., and Fernandez Luna D.: El sindrome endócrino-hépato-cardiaco de la hemochromatosis, Rev. Asoc. méd. argent. 52: 1015, 1938.
19. de Vēricourt, R.: Le Syndrome endocrino-hépato-myocardiaque, Theses de Paris 1: 144, 1935.
20. Butt, H. R., and Wilder, R. M.: Hemochromatosis. Report of 30 Cases in Which Diagnosis Was Made During Life, Arch. Path. 26: 262, 1938.

BIDIRECTIONAL PAROXYSMAL TACHYCARDIA: TOXICITY OF DIFFERENT CARDIAC GLYCOSIDES

L. Braun, M.D., and P. H. Wosika,* M.D., Ph.D.
Chicago, Ill.

INTRODUCTION

PAROXYSMAL ventricular tachycardia is rare,[1, 2] and the bidirectional variety is even rarer.[3, 4] We have obtained records of the beginnings and endings of a number of long paroxysms. Since only a fraction of the published curves register these onsets and terminations, we feel justified in reporting this case, even though numerous controversial points concerned with the origin and mechanism remain unsolved. Clinically, the solution of these points can be approached only by analysis of the electrocardiographic pattern of a large number of tracings, including the onsets and terminations.

The role of digitalis in the causation of paroxysmal ventricular tachycardia is well known. In our case we demonstrated an apparently selective toxic sensitivity to *Digitalis purpurea* which was in marked contrast to the beneficial effect of strophanthin in controlling failure; the patient tolerated *Digitalis lanata,* which has maintained compensation.

This case is also interesting because of the length of life (twenty-seven months) after the attack, in view of the serious prognosis, if not terminal condition, that these paroxysms usually portend.

CASE REPORT

C. S., a 68-year-old construction engineer, was admitted to the Illinois Masonic Hospital Nov. 20, 1942. The family history revealed serious cardiorenal vascular disease on both sides; the patient was the only survivor. His past history revealed long and hard years of work. In 1935 (at the age of 61 years) he had an attack of pain in the chest radiating into the shoulders. After two weeks in bed he returned to work and remained under medical supervision, receiving varying and unknown amounts of digitalis. In 1936 an electrocardiogram showed auricular fibrillation and evidence of severe myocardial damage (Fig. 1, *A*). In 1941 (at the age of 67 years), he had what was possibly a pulmonary embolus after a hemorrhoidectomy. This delayed his convalescence ten days. In May, 1942, he had several boils which were treated surgically and successfully. However, by June he was short of breath, he started to cough, and he noted swelling of the ankles. In spite of numerous variations in the dosage, type, and mode of administration

Read by title at the Sixteenth Annual Meeting of the Central Society for Clinical Research, Chicago, Nov. 5, 1943.
Received for publication Nov. 1, 1943.
*From the Departments of Medicine of the Illinois Masonic Hospital and The Chicago Medical School, Chicago.

of digitalis, his symptoms worsened progressively until he was admitted to the hospital in a critical condition. As far as could be ascertained, digitalis had been stopped on Oct. 18, 1942.

Physical examination revealed an orthopneic, cyanotic, grossly edematous man, seriously ill. The tongue was dry. The neck veins were distended and pulsated irregularly. Numerous râles were present throughout both lungs. The heart was markedly enlarged; the apex beat was diffuse. Auricular fibrillation was present: the apical rate was 120, and the radial, 86. No murmurs were heard, but occasional accentuation of the muffled heart tones aroused the suspicion that ectopic beats were present. The blood pressure was 145-150/110-120. The abdomen was distended, and the edge of the liver was firm, tender, and 2 inches below the costal margin. Although no free fluid was demonstrated in the abdomen, there was marked edema of the abdominal wall, extremities, and serotum. His weight was 210 pounds.

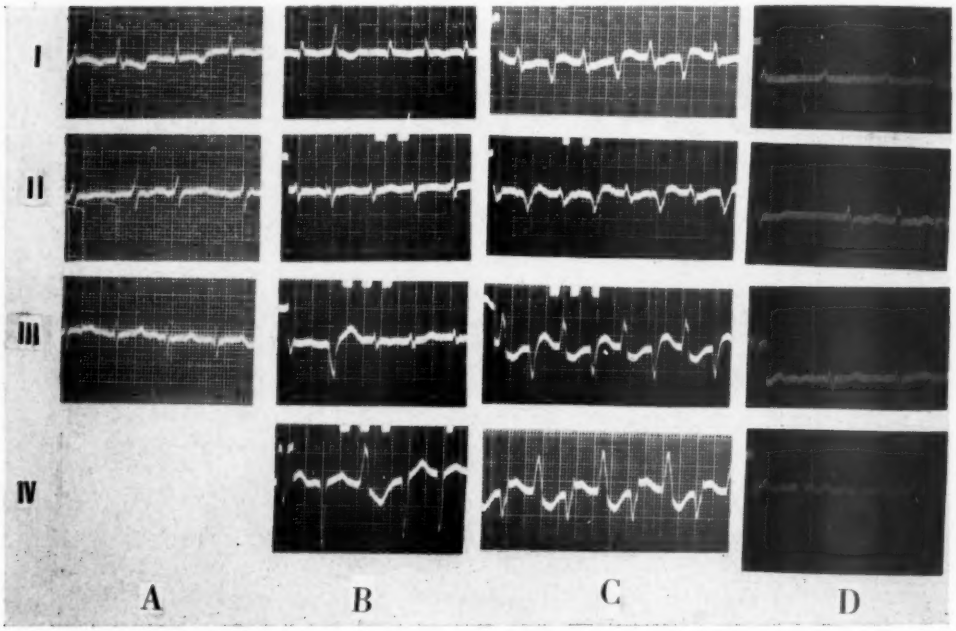
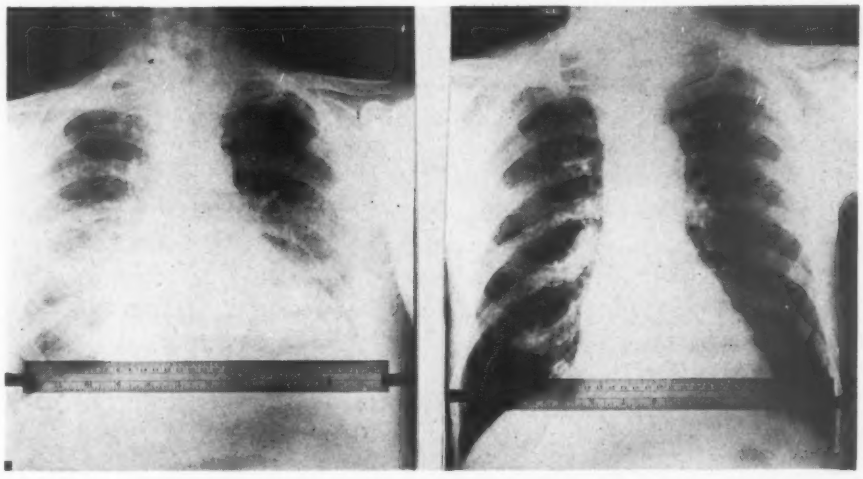


Fig. 1.—*A* shows the extremity leads in 1936; *B* shows four leads upon admission to hospital Nov. 20, 1942; *C* shows electrocardiographic appearance at the height of the bidirectional paroxysmal ventricular tachycardia; *D* shows the electrocardiogram in June, 1943.

The electrocardiogram (Fig. 1, *B*) showed auricular fibrillation with a ventricular rate of approximately 130, ectopic ventricular systoles, left axis deviation, low voltage of the QRS complexes, and flattening of the T waves such as occurs with serious myocardial damage. The teleoroentgenogram (Fig. 2, *A*) showed the following measurements: M R* = 7.5 cm., M L† = 14.6 cm., and transverse diameter of chest, 30.6 centimeters. According to the Ungerleider and Clark[5] method, the theoretical value for the total diameter should not exceed 123 millimeters.

*M R = midline to right border.
†M L = midline to left border.

The patient's weight while he was at rest in bed increased 10 pounds in two days. Since he had received no digitalis for thirty-five days, he was given 12 cat units of *Digitalis purpurea* on November 22, 4 cat units on November 23, and 6 cat units on November 24, all in divided doses, when the first paroxysm of alternating ventricular tachycardia was discovered (Fig. 1, *C*) and the digitalis was stopped. These attacks subsided within two days, but the edema increased and Cheyne-Stokes breathing became more marked, with apneic periods lasting almost sixty seconds. The patient's condition was considered hopeless. Oxygen was administered constantly. Mercupurin in ⅓ c.c. or ½ c.c. doses was given almost daily with unpredictable effect. Because of the patient's poor condition and continued auricular fibrillation, it was decided to administer digitalis in smaller doses in an attempt to slow the rapid ventricular rate. Accordingly, 1 cat unit was given at approximately twelve-hour intervals from November 29 until December 5, when attacks of paroxysmal tachycardia similar in type to that shown in Fig. 1, *C*, recurred.



A. *B.*

Fig. 2.—Shows the teleoroentgenogram taken; *A*, upon admission, and *B*, upon discharge.

Quinidine sulfate was started (3 grains) on December 11. This dose was increased to 9 grains on December 12, 12 grains on December 13, and 18 grains on December 14 without appreciable improvement. On December 15, this dosage was reduced to 9 grains daily, and 0.125 mg. of strophanthin was administered intravenously. From December 16 to December 23, strophanthin was given in a dose of 0.25 to 0.50 mg. daily. At this time the patient developed an upper respiratory infection (pulmonic infarction?), and his temperature was elevated. In spite of this, he improved, as was shown by a slowing of the ventricular rate and a diminution in the pulse deficit. At this time he was receiving 6 grains of quinidine and 0.125 mg. of strophanthin, at first daily and then intermittently, and occasional ½ c.c. doses of mercupurin; this completed the dehydration process. On January 12, the patient weighed 148 pounds, i.e., he had lost 72 pounds. On January 18, *Digitalis lanata* (1 cat unit daily) was substituted for the strophanthin. Roentgen-

ologically (Fig. 2, *B*), there was a decrease in the pulmonary congestion and in the size of the heart shadow. The measurements were: M R = 4.9 cm., M L = 12 cm., and total diameter of the chest, 31.4 centimeters. He was discharged from the hospital in a greatly improved condition on Feb. 14, 1943, seventy-six days after admission.

At home the *Digitalis lanata* was reduced to 1 cat unit every second or third day, and the quinidine discontinued. The patient continued to gain in strength. In June the *Digitalis lanata* was stopped, and, although his weight did not change, the apical rate increased almost 20 beats per minute. Therefore, the small doses were resumed. The electrocardiogram (Fig. 1, *D*) showed a continuation of the low voltage and evidence of myocardial damage. Only occasional ectopic beats were noted.

The patient is up and about. Occasionally, he has even returned to business. During the entire period he has been maintained upon a modified acid-ash, low-sodium diet, with 6 to 9 Gm. of ammonium chloride daily. At no time during his illness did numerous blood chemical values deviate from the normal.

COMMENT

This patient was both interesting and instructive. It would seem that he had myocardial infarction in 1935, and that this caused the auricular fibrillation. The electrocardiogram in 1936 (Fig. 1, *A*) substantiates this diagnosis. He was symptomless, however, until the series of furuncles developed in 1942, after which cardiac decompensation appeared. It is not known whether there were attacks of ventricular tachycardia previous to his hospitalization. Failure, however, increased, and digitalis must have been suspected as a cause because the drug had been discontinued.

After admission, the increasing degree of congestive failure while he was in bed, the auricular fibrillation with rapid ventricular rate, and assurance from the family physician and the patient's own records that no digitalis had been received for five weeks prompted the administration of digitalis. We were not in possession of the 1936 electrocardiogram at the time, and we felt that the auricular fibrillation was a recent development, coinciding with the decompensation. *Digitalis purpurea* administration led to attacks of ventricular tachycardia which ceased when the drug was discontinued, and reappeared upon resumption of the drug. Quinidine was then given, despite the apparently diffuse, serious myocardial lesion, and without much hope of either establishing normal rhythm or having much effect upon the ventricular contractions.[6] The ventricular rate remained rapid, and there was no effect upon the number of ectopic beats, the Cheyne-Stokes breathing, or the edema.

Unequivocally, all of the indications for digitalization remained the same. Oettel,[7] investigating the so-called "paradoxical action" of the digitalis glycosides (increase in the sinus rate and appearance of ectopic beats), pointed out the lesser toxicity of the strophanthin series. In this respect, the lanata glycosides have been considered superior to the purpurea glycosides.[8] Accordingly, we administered strophanthin in

doses increasing from ⅛ to ½ mg. daily; this was well tolerated, and improvement was steady and gratifying. We are unable to say that a beneficial synergism existed between the quinidine and strophanthin, although we realize the possibility. When the patient had improved sufficiently, *Digitalis lanata* was administered with gratifying results. This was done to avoid continuous intravenous therapy.

Throughout the entire period of observation, we were impressed by the lack of relationship between the amount of mercurial diuretic given and the subsequent urinary output. Small doses, of ⅓ c.c., and even less, are safer and are superior[9] to large doses. The total urinary output after eight ¼ c.c. doses, given upon alternate days, invariably exceeds the response obtained from 2 c.c. given in one dose.[10] The important feature is the state of the circulation, which was stressed by earlier writers upon the subject. In our case ammonium chloride was given throughout the entire hospitalization in doses of 6 to 9 Gm. daily.[11] During the first period of digitalization a fair but unreliable diuretic effect of the mercurial was observed, quite independent of the amount injected and with noticeable ineffectiveness during the periods of the paroxysms. The diuretic effect was poor when the mercurial was given with quinidine. Simultaneous or previous administration of aminophyllin by mouth or intravenously was without effect.[12] During the time of the first doses of strophanthin, the effect was poor; it was adequate and reliable, depending on whether an improved circulation was maintained by strophanthin or *Digitalis lanata*.

Ventricular tachycardia is a serious disturbance, and the bidirectional type is considered to be fatal.[13] The prognosis varies with the seriousness of the underlying cardiac lesions. In spite of the enlargement and dilation of the heart, possible pericardial effusion, myocardial infarction, coronary sclerosis, hypertension, and auricular fibrillation, this patient may still be in Class III according to the Criteria Committee of the New York Heart Association,[5] twenty-seven months after the attacks of tachycardia.

The electrocardiographic appearance of the paroxysm at the height of the attack is shown in Fig. 1, *C*, during which regularly alternating complexes may be observed. The rate approximated 160 per minute.

Fig. 3 shows the electrocardiographic appearance between the paroxysms (*A*, *D*, *E*, *H*, and *K*), the onsets of the paroxysms in four leads (*B*, *F*, *I*, and *L*), and the endings in the extremity leads (*C*, *G*, and *J*).

The auricles are fibrillating, and, in Lead I, the ventricular rate (Fig. 3, *A*) is about 100 per minute, which is slower than was noted upon admission (Fig. 1, *B*). The QRS complexes are of low voltage and the T waves are practically isoelectric. This supraventricular mechanism is interrupted by an ectopic systole of right ventricular origin, the coupling time of which cannot be measured exactly. This ectopic beat is similar to, but is not exactly the same as, the one observed upon admission

(Fig. 1, *B*, Lead I). Whether this difference is due to a digitalis effect cannot be stated with certainty. The rate is slower and the possibility of a fusion beat has to be considered. In Fig. 3, *B*, the paroxysm begins with a premature beat, the coupling time and contour of which are similar to the one in Fig. 3, *A*. The main deflection of the second complex is directed downward. The next five complexes show irregularities in shape, direction, and rate. These variations may be due to (a) origin of the stimulus in the ventricles from multiple foci; (b) origin from one focus with aberrant pathways; or (c) fusion (interference)[14, 15] phenomena. After the first seven complexes, the regular bidirectional tachycardia evolves, as is shown in Fig. 1, *C*. It is to be noted that there is a definite difference between the shape of the upwardly directed complexes at the onset and in the middle of the paroxysm. In *C*, the end of a paroxysm is shown. The rate slows gradually, just as it increased speed gradually after the onset. After the first complex shown, irregularities appear, i.e., two consecutive upwardly directed complexes are present, in this instance partly obscured by the standardization. The eighth complex comes "prematurely," is aberrant, and is followed by a "compensatory pause" (the distance between the seventh and ninth complexes, measured from the point where the trace leaves the base line, is very close to the distance between the fifth and seventh) before the next upwardly directed deflection occurs. This pause is followed by a blunted complex which is followed by a still longer pause, roughly equal in time to that noted in Fig. 3, *G* and *J*. A bizarre, widened complex (number 11) may represent a fusion beat. After a definite supraventricular complex, a pair of alternating extrasystoles occurs, the first of which is upright, after which the mechanism returns temporarily to auricular fibrillation.

In Lead II of Fig. 3, a single premature ventricular systole is shown in *D*, and a similar complex is seen in E, followed closely by another premature beat of a different configuration; these are the same two forms that appear to initiate the paroxysm in *F*. The coupling time of this extrasystole is different in *D*, *E*, and *F*. In *F*, the third complex is broadened, is distinctly downward, and is similar in form to that noted at the height of the paroxysm. After two alternating complexes the form changes abruptly and completely to unidirectional tachycardia with a rate of approximately 150 per minute. Near the end of this paroxysm (not shown in Fig. 3) the rate gradually slowed, the shape gradually returned to that of the third and fifth complex, and the paroxysm ended with a somewhat premature contraction, suggesting interference, after which the supraventricular rhythm was restored. This unidirectional variation was unusual, and was recorded upon one occasion only. The typical alternating complexes in Lead II may be seen in Fig. 1, *C*. In Fig. 3, *G*, a slight slowing of the tachycardia may be observed, and two downwardly directed complexes occur which herald the end without further irregularities.

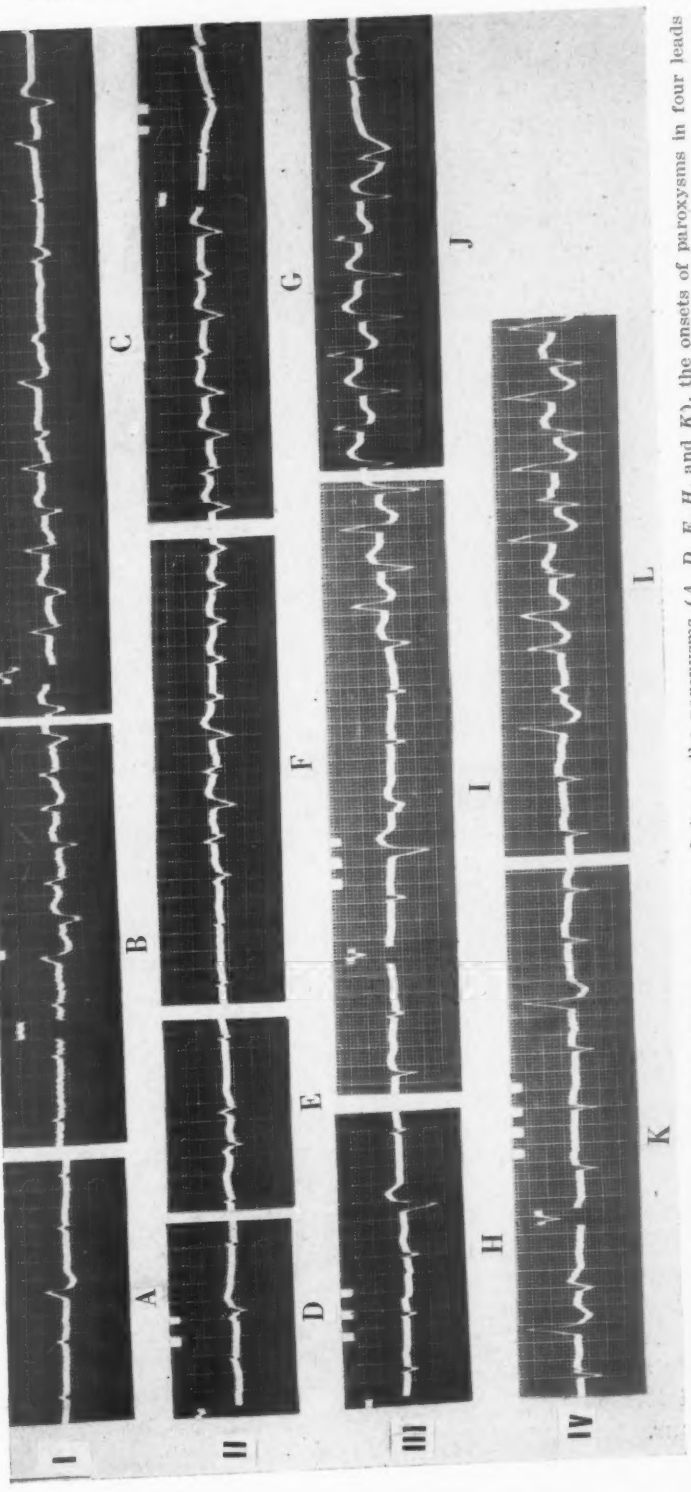


Fig. 3.—Shows the electrocardiographic pattern of sections between the paroxysms (*A*, *D*, *E*, *H*, and *K*), the onsets of paroxysms in four leads (*B*, *F*, *I*, and *L*), and endings in the extremity leads (*C*, *G*, and *J*).

In Lead III (Fig. 3, *H*) a downwardly directed premature systole is shown. This is similar in contour to the extrasystole noted in Lead III (Fig. 1, *B*), taken upon admission, the fifth complex in *I*, and the downwardly directed complex during the height of the paroxysm. In *I*, the first deflection is an extrasystole similar to the one which initiates the paroxysm. In this onset no such major irregularities occur as were noted in *B* and *F*, although, in other strips, these were noted frequently. Toward the end (*J*) the rate slows slightly, and again a pair of inverted complexes appears. The final complex is deformed somewhat by a movement of the string.

Lead IV (Fig. 3, *K*) shows a pair of alternating and a single premature ventricular contraction. The upwardly directed complex is quite similar to the one recorded upon admission (Fig. 1, *B*), the one preceding the paroxysm (*L*), and the upwardly directed complexes during the height of the paroxysm (Fig. 1, *C*). In *L* two upright complexes occur, after which the bidirectional tachycardia is established with gradually increasing rate. The inverted complexes are seen to change shape gradually during the first few beats. The termination of this paroxysm was not recorded.

Briefly, the following points may be made after study of the electrocardiograms:

1. The most often encountered premature ventricular systole was of the right ventricular type, originating below the bifurcation. This extrasystole was similar to the one originating the tachycardia, yet it was not identical to the complex present during the height of the paroxysm.

2. This premature beat appeared alone, or was followed either by an alternating complex (Fig. 3, *C* and *E*) or another aberrant (fusion?) form (Fig. 3, *I*).

3. The coupling time of this premature complex with the preceding supraventricular complex was variable, which makes a re-entry theory difficult to defend.

4. The longest coupling time was longer than the shortest distance between two supraventricular complexes. Thus, an aberrant pathway alone could not account for the shape of the extrasystole if it originated above the bifurcation.

5. In spite of the difficulty in measuring the prematurity of these contractions because of the underlying auricular fibrillation, the pause that followed these ectopic beats was longer than the usual distance between two supraventricular contractions, and appears "compensatory."

6. There was a striking regularity of the alternating complexes in the middle of the paroxysms; there was a definite irregularity at the onset and termination, consisting of irregularities of rate, alternation, and contour.

7. The ends of the paroxysms showed no definite pattern except a gradual slowing of the rate and a rather long "compensatory" pause before the supraventricular complexes reappeared.

8. Impairment of conduction might explain minor variations in the size and shape of the complexes, but it is hard to explain the regular alternation of complexes at the height of the paroxysm simply upon this basis. Impairment of conduction should be accompanied by more variations in the configuration of the complexes.[16]

9. A simple or modified figure-of-eight circus wave, besides lacking experimental evidence and an anatomic basis, should be extinguished by the premature beat in Fig. 3, *C*, yet the upward complex appeared again.

10. Measurements of the distance between cycles was very unreliable, even in parts of the curve that were technically perfect. Irregularities of rate could not be demonstrated by measurement during the height of the paroxysm.

11. In view of these observations, it would seem that numerous ectopic foci in the ventricular myocardium below the bifurcation produced the bidirectional ventricular tachycardia, either by a fusion phenomenon or by the domination, eventually, of two centers of similar rates during the height of the paroxysm.

SUMMARY

A case is reported in which a series of attacks of bidirectional ventricular tachycardia followed, upon two occasions, the use of *Digitalis purpurea*. Strophanthin and *Digitalis lanata* produced no such toxic effects.

Study of the electrocardiograms in this case does not substantiate the currently favored theories of the origin of this disturbance. The assumption that multiple ectopic foci are present in the damaged myocardium and are responsible for this alternating paroxysmal ventricular tachycardia cannot be avoided. The height of the paroxysm may be the result of interference phenomena, or of the predominance of two centers of the same order over the other ectopic foci, evidence for which may be seen at the beginnings and endings of the paroxysms. Such a theory has the advantage of explaining the different forms of paroxysmal tachycardia.

REFERENCES

1. Cooke, W. T., and White, P. D.: Paroxysmal Ventricular Tachycardia, Brit. Heart J. 5: 33, 1942.
2. Williams, C., and Ellis, L. B.: Ventricular Tachycardia. An Analysis of Thirty-six Cases, Arch. Int. Med. 71: 137, 1943.
3. Marvin, H. M.: Paroxysmal Ventricular Tachycardia With Alternating Complexes Due to Digitalis Intoxication, AM. HEART J. 4: 21, 1928.
4. Scherf, D., and Kisch, F.: Ventricular Tachycardias With Variform Ventricular Complexes, Bull. New York M. Coll., Flower & Fifth Ave. Hosps. 2: 73, 1939.

5. Nomenclature and Criteria for Diagnosis of Diseases of the Heart, ed. 4, New York, 1939, New York Heart Association.
6. Kerr, W. J.: Use of Quinidine in Cardiac Irregularities. The Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, vol. III, p. 474.
7. Oettel, H.: Ueber "paradoxe Digitaliswirkung." Ein Beitrag zur Beziehung zwischen chemischer Konstitution und biologischer Wirkung der Herzglucoside, Zeit. f. d. ges. exper. Med. **108**: 713, 1941.
8. Stoll, A.: The Genuine Cardiac Glucosides, J. Am. Pharm. A. **27**: 761, 1938.
9. Fitz, R.: Edema and Its Management. Proceedings of the International Assembly of the Inter-State Post Graduate Medical Association of North America, Chicago, 1940, p. 100.
10. Unpublished personal observations.
11. Vollini, I. F., Levitt, R. D., and Campione, N. L.: Studies on Mercurial Diuresis. IV. Ammonium Chloride: The Evaluation of Its Clinical and Chemical Effects, Illinois M. J. **84**: 107, 1943.
12. Goodman, J. I., Corsaro, J. F., and Stacy, R.: Mercurial and Xanthine Diuretics in Chronic Congestive Heart Failure, Arch. Int. Med. **70**: 975, 1942.
13. White, P. D.: Heart Disease, New York, 1937, The Macmillan Co., p. 624.
14. Katz, L. N.: Electrocardiography, Philadelphia, 1941, Lea and Febiger.
15. Scherf, D., and Boyd, L. J.: Clinical Electrocardiography, St. Louis, 1940, The C. V. Mosby Co.
16. Wenckebach, K. F., and Winterberg, H.: Die unregelmässige Herztätigkeit, Leipzig, 1927, Wilhelm Engelmann.

Abstracts and Reviews

Selected Abstracts

Holt, J. P.: The Effect of Positive and Negative Intrathoracic Pressure on Cardiac Output and Venous Pressure in the Dog. Am. J. Physiol. **142**: 594, 1944.

Cardiac output was measured by the direct Fick method and by a modification of Stewart's method in dogs breathing oxygen and air at pressures of 8 and 16 cm. of water below atmospheric, 8 and 16 cm. of water above atmospheric, and at atmospheric, pressure. The control cardiac output determinations made with the Fick method showed considerable variation, while the control determinations with the modified Stewart method showed little variation. The cardiac output determinations with the modified Stewart method showed that, when air under a positive pressure of 16 cm. of water was breathed, the cardiac output was decreased. The average decrease was 33 per cent of the control. When air under a negative pressure of 16 cm. was breathed there was little change in the cardiac output.

Peripheral venous and right auricular pressures were measured simultaneously in dogs breathing air from a chamber in which the pressure varied from 20 cm. of water pressure above, to 20 cm. below, atmospheric pressure. When air under a positive pressure of 16 cm. of water was breathed, the pressure fall from peripheral vein to right auricle was decreased. The average decrease was 72 per cent of the pressure fall when air under atmospheric pressure was breathed in one group of experiments and 64 per cent in another. When air under a negative pressure of 16 cm. of water was breathed, the pressure fall from peripheral vein to right auricle increased. The average increase was 191 per cent of the control pressure fall in one group of experiments and 244 per cent in another.

Since the cardiac output of the dog changes very little when air under a negative pressure of 16 cm. of water is breathed, it would appear that the maintenance of a high peripheral venous pressure, when right auricular pressure is greatly decreased, is due to the fact that the veins become partially collapsed just before entering the chest and increase the resistance to the flow of blood to the right auricle.

AUTHOR.

Forero, A., Silva, R., and Saffie, F.: Electrocardiographic and Anatomical Studies of Experimental Precordial Trauma. Rev. argent. de cardiol. **11**: 77, 1944.

The authors studied the effect of precordial trauma on twenty-one cats. Many electrocardiographic curves were made in each one of them, before and after the trauma. Then the animal was killed and a macroscopic study of the whole heart and a microscopic study of the interventricular wall were made. The various factors which can influence the electrocardiographic curves and the anatomic alterations were studied. The final conclusions of this experiment were as follows:

Experimental precordial trauma on the cats produces electrocardiographic and anatomic alterations of the heart.

To a certain extent, the intensity of anatomic alterations is parallel to the violence of the blow. But many other factors play an important role, as elasticity of the thorax, cardiac and respiratory phase when the blow is applied, etc. As a consequence we can observe that equally intensive blows produce anatomic damage of different magnitude.

Precordial trauma produces various electrocardiographic alterations and is not related to the localization or the intensity of the anatomic damage. Sometimes it is possible to find electrocardiographic alterations and no apparent anatomic damage which might be attributed to a phenomenon of cellular commotion.

The results of this experimental study demand further investigation in the cardiac aspects of our patient of precordial trauma. They also suggest a careful investigation into the traumatic background of some cardiac patients whose etiological factors remain unknown.

AUTHORS.

Moses, C., and Ferderber, M. B.: The Oscillometer and Thermocouple as Diagnostic Aids in Peripheral Vascular Disease. J. Lab. & Clin. Med. **29**: 1147, 1944.

Observations relative to the peripheral circulation were made on one hundred two individuals. This group included forty-eight normal subjects, eight asymptomatic, six with thromboangiitis obliterans, and twenty-eight with arteriosclerosis. Observations as to history, symptoms, physical signs, oscillometric readings, skin temperatures, blood flow, and vibratory sensation were noted, and the results tabulated.

The techniques used in obtaining the data are briefly described.

While in arteriosclerosis of the lower extremity, symptoms referable to the calf were most common, pain was noted almost as frequently in the ankle, arch, dorsum, or toes. Numbness, tingling, burning, aching, and rest pain were symptoms noted almost as frequently as intermittent claudication in arteriosclerotic vascular disease. A feeling of local fatigue was often the first sign of vascular disease.

Arteriosclerotic rest pain was often relieved by moderate exercise. The pain of thromboangiitis obliterans was not relieved by exercise in any of our patients.

Normal distribution of the hair over the lower extremity was noted in only 25 per cent of the patients with vascular disease.

Rubor, cyanosis, or pallor of an extremity may be present in the absence of arterial vascular disease.

The absence of the dorsalis pedis or posterior tibial pulsation was not pathognomonic of vascular disease, and the presence of a pulsation did not exclude vascular pathology.

The oscillometric readings were not necessarily found to be decreased in arteriosclerotic peripheral vascular disease; normal individuals with heavy musculature may have diminished oscillometric readings.

Normal skin temperatures may obtain in individuals with vascular disease.

Estimation of the blood flow by Stewart's calorimetric method indicated that the blood flow in patients with vascular disease averaged about two-thirds of that in normal subjects.

Estimation of the vibratory sense by the method of Barach yields confirmatory evidence of deficient circulation but is of little early diagnostic value.

The arteriolovenous anastomoses are suggested as one mechanism partially explaining the variations in skin temperature that occur in normal individuals and those with peripheral vascular disease.

AUTHORS.

Paley, S. S., and Krell, S.: Fetal Electrocardiography and Stethography. Am. J. Obst. & Gynec. **48**: 489, 1944.

An attempt was made to record fetal electrocardiograms and stethograms in twenty-one gravid women of varying periods of gestation. Positive fetal electrocardiograms were obtained in 53 per cent; positive stethograms were obtained in 79 per cent. Where large fetal electrocardiographic deflections were obtained they were diphasic, otherwise they were single downward spikes in all but one case. The latter was probably a breech presentation at the time the record was made.

The weight of the mother and size of the fetus influence the successful demonstration of the fetal electrocardiogram, but the age of the mother, her parity, fetal presentation, and fetal sex are not factors in determining the production of fetal electrocardiographic deflections. The fetal cardiac rate bears no relationship to its sex; limb leads are of no value in obtaining fetal electrocardiograms; the best abdominal leads were those connecting the fundus of the uterus with the symphysis pubis; the pattern of a fetal stethogram resembles that of the adult; and the configuration of the sounds assumes the form of M, N, or W. The term embryocardia is a misconception.

AUTHORS.

Parkinson, D., Posch, J. L., and Stofer, B. E.: Tricuspid Mitral Valve: A Report of a Case, With a Suggestion as to the Mode of Development. Arch. Path. 38: 222, 1944.

A tricuspid mitral valve unassociated with any other congenital defects was observed in a 77-year-old farmer. The anterial lateral and medial cusps of this heart represent an incompletely fused anterial mitral cusp, and the posterior cusp, which is normally the smaller, represents the true posterior mitral leaflet.

AUTHORS.

Capaccio, G. D.: The Electrocardiogram After Exercise in Angina Pectoris. Northwest Med. 43: 144, 1944.

The electrocardiogram after exercise in angina pectoris is offered as an additional objective observation to confirm the clinical opinion. A negative (response to the exercise) test does not rule out the diagnosis of angina pectoris.

AUTHOR.

Feasby, W. R.: Rheumatic Fever in the Canadian Army. War Med. 6: 139, 1944.

About 4 per cent of persons with streptococcic disease of the respiratory tract acquire polyarthritis. The incidence of polyarthritis follows closely the incidence of streptococcic disease of the respiratory tract. Ninety per cent of the cases occurred in the first seven months of the year. Military populations most seriously affected were those of Saskatchewan and Alberta. No particular strain of streptococci accounts for these cases or their complications. The commonest type was A 19, which was predominant in the 1943 streptococcic epidemic at Camp Borden, Ontario.

From an analysis of four hundred seven such cases from the Canadian Army in Canada for 1943, it was found that (a) 24 per cent of the patients had cardiac complications, (b) 23 per cent are on full duty one year later, (c) 17 per cent are on low pulhems duty, and (d) 60 per cent are discharged and may be pensioned. The estimated cost for this group of cases is nearly $6,000,000 to be expended over the next thirty years. Approximately $700,000 has been spent to date for the 1943 cases.

Preventive measures include proper dust control in sleeping quarters and adequate hospital isolation of persons with streptococcic illness.

AUTHOR.

Wedum, A. G., and Wedum, B. G.: Rheumatic Fever in Cincinnati in Relation to Rentals, Crowding, Density of Population, and Negroes. Am. J. Pub. Health 34: 1065, 1944.

This survey again emphasizes the importance of poverty and crowding in the genesis of rheumatic fever. However, poverty and crowding are only signposts pointing to a more fundamental epidemiological principle. It is instructive to com-

pare the information gained by such surveys as this with what is now known about rheumatic infections in military camps in the United States. There is a comparatively high incidence of rheumatic fever in the military forces in Colorado, Idaho, and Utah. These camps are in dry areas, removed from water courses, and at relatively high altitudes. Needless to say, poverty is no factor, and the housing, sanitation, and diet are excellent. In fact, there are only two features common both to the military forces in these states and to the impoverished civilians in areas with a high incidence of rheumatic fever, namely, (1) crowding and (2) inability to control the micro-climate. It is not always possible for either the poor man or the military man to rest whenever he is tired, get warm when he is cold, and keep dry when it is raining. In civilian life, poverty, diet, proximity to water courses, etc., might be said to be important only in so far as they are a part of the two features mentioned, and so reduce the power of the body to resist disease.

AUTHORS.

Paulley, J. W., and Aitken, G. J.: Case of Cardiovascular Beri-Beri. Lancet 2: 440, 1944.

A case of cardiovascular beriberi is described. Three etiological factors may be recognized: (a) marginal, and submarginal diet; (b) some alcohol, but not chronic alcoholism; and (c) possibly age. The patient presented the usual clinical features of cardiovascular beriberi, and showed a grossly deficient excretion of vitamin B_1. Circulation time (arm-lung) was abnormally long. Recovery was clinically complete in forty days.

AUTHORS.

Leiper, E. J. R.: Hypertension Associated With Unilateral Renal Lesion. Lancet 2: 439, 1944.

The question arises whether recovery was due to the removal of the diseased kidney, and what part, if any, was played by the right-sided sympathectomy. The evidence suggests, I think, that the role of the sympathectomy was insignificant, and that the benefit must be ascribed to the nephrectomy. Judging by the results of widespread bilateral removal of sympathetic ganglia and fibers (Jefferson, 1942; Takats et al., 1942), the dramatic cure here witnessed could scarcely have been the result of sympathectomy confined to one side. Nephrectomy, on the other hand, when successful, is usually strikingly so.

When a unilateral renal lesion is found in a patient with hypertension it does not by any means follow that the hypertension will disappear on removal of the kidney. The number of cures so far recorded is small.

AUTHOR.

Bigger, I. A.: Treatment of Traumatic Aneurysms and Arteriovenous Fistulas. Arch. Surg. 49: 170, 1944.

Twenty-nine cases of traumatic arterial aneurysm or arteriovenous fistula have been studied. Unfortunately, satisfactory follow-up studies have not been possible in a considerable number of cases but it is believed that evidence of some value has been obtained regarding the occurrence of subjective symptoms of chronic circulatory deficiency after obstruction of main arteries of the extremities. Eight of nine patients in whom one of the main arteries to the lower extremity was obstructed had follow-up examinations at periods of from nine months to eight years after operation. Seven of them have definite symptoms of chronic circulatory deficiency distal to the obstruction.

Excision of an aneurysmal sac is more certain to cure the lesion than aneurysmorrhaphy but has the disadvantage of destroying more collateral channels than does the intrasaccular operation. It is more reasonable to assume that interference with the

collateral arteries would increase the danger of ischemic gangrene and would also increase the degree of chronic circulatory deficiency.

An atypical or incomplete operation may result in cure of a traumatic aneurysm, but an arteriovenous fistula is rarely cured except by complete ligation of the involved vessels and excision of the fistulous area or by suture of the artery. If the latter procedure is employed it is usually better to ligate the vein above and below the fistula and then to open the vein and suture the artery under direct vision.

Evidence is also presented which indicates that while the excellent collateral circulation developed in the presence of an arteriovenous fistula makes the danger of ischemic gangrene almost negligible, it does not prevent persistent circulatory difficulty when main vessels are ligated and resected. It is therefore suggested that, when such important vessels as the carotid artery and jugular vein, the common femoral vessels, or the popliteal vessels are the site of arteriovenous fistula, transvenous repair of the artery be employed if there are no contraindications. The most important contraindication to arterial suture is calcification of the wall of the artery in the area to be sutured.

When the main vessels are obstructed, especially those to the lower extremity, permanent interruption of the sympathetic nerves to that extremity may help prevent chronic circulatory deficiency distal to the obstruction.

AUTHOR.

Green, H. D., Dworkin, R. M., Antos, R. J., and Bergeron, G. A.: Ischemic Compression Shock, With an Analysis of Local Fluid Loss. Am. J. Physiol. **142**: 494, 1944.

An ischemic trauma was produced by application of rubber tubes in the form of a tight continuous spiral bandage from the ankle to the groin of both hind legs of dogs anesthetized with morphine and sodium pentobarbital. Upon release of the tubes after 6 or more hours compression, death occurred in twenty-four of a first group of twenty-five minimally anesthetized dogs which were free to move about in their cages, and in all of a second group of fourteen dogs anesthetized for longer intervals and restricted to animal boards in a supine position. The dogs of the first group survived 0.8 to 50 hours after release of the rubber tubes, with an average survival of 11.8 hours. The dogs of the second group survived 2 to 20 hours with an average survival of 7.9 hours.

Following the release of the rubber tubes the mean arterial pressure in the dogs of the second group fell rapidly from around 170 to 180 mm. Hg to around 120 to 150 mm. Hg accompanied by a marked rise in heart rate, and a reduction of blood flow in the forepaws, as indicated by subcutaneous temperature records. The mean arterial pressure then declined more slowly to about 50 to 60 mm. Hg, after which death from respiratory or cardiovascular failure ensued within a relatively few minutes. Collapse of the peripheral veins was noted during the period of declining arterial pressure. The hematocrit reading rose rapidly during the first hour after removal of the rubber tubes and continued to rise slightly during the ensuing hours. Depression of activity and sluggish response to stimulation were seen in the lightly anesthetized dogs after release of the limb compression.

The accumulation of fluid in the traumatized extremities was measured by immersion of the legs separately in a suitable tall narrow vessel before applying the rubber tubes and again after death. After allowing 5 ml. per kilogram of dog per extremity for shrinkage of the legs with death, and after allowing for the fact that immersion may measure only 91 per cent of the true edema, the estimated maximum volume of edema still ranged from 15 to 56, with an average of 41.3 ml. per kilogram of body weight in the dogs of the first group and from 3.3 to 33 with an average of 17.6 ml. per kilogram of body weight in the second group of experiments. One leg only was traumatized in seven dogs. Three of these died with an estimated maximum volume of edema of 33, 33, and 55 ml. per kilogram. The remaining four

were killed at approximately twenty hours. The estimated maximum edema in these dogs was 20 to 47 ml. per kilogram of dog.

The above observations are not explainable on the basis of a reactive hyperemia in the traumatized legs alone. Accumulation of fluid in the legs is apparently an important factor in the induction of the shock state, but in many of the experiments the volume of edema appears to be insufficient of itself to explain the death. If the operation of humoral or nervous factors are not subsequently demonstrated to play a part in the induction of this type of shock we may have to revise downward our estimates of the quantity of local edema necessary to induce shock, especially in the absence of hemorrhage into the traumatized tissues.

The somewhat shorter survival and lesser edema in the second group of dogs demonstrates the importance of prolonged anesthesia and of restriction of activity in contributing to the ease with which shock with fatal outcome may be induced. Evidence is presented which suggests that dogs studied in the spring resist shock better than do dogs studied during the winter months.

AUTHORS.

Mazer, M., and Wilcox, B. B.: A Simple Graphic Method for Measuring the Area of the Orthodiagram. Am. J. Roentgenol. **51**: 444, 1944.

A simple graphic method for the determination of the area of the orthodiagram is described. It requires no equipment not readily available to any physician. Its application to one hundred cases checked by the planimeter shows it to have a sufficiently high degree of accuracy for clinical purposes.

AUTHORS.

Reynolds, J. T., and Jirka, F. J.: Embolic Occlusion of Major Arteries. Surgery **16**: 485, 1944.

Heparin should be administered as soon as the diagnosis of arterial embolus is made. This is done in order to prevent a thrombosis of the blood distal or central to the embolus, which, should it occur, would make all attempts to restore blood flow futile.

Sympathetic block should not be used in aortic, iliac, or femoral embolic occlusion until the operation has been done, because the resultant vasodilatation may allow the clot to progress and escape into vessels from which it can no longer be removed with ease.

Embolectomy should be done as soon as possible after diagnosis.

Most occlusions of the femoral and iliac arteries and the aorta may be satisfactorily displaced by approach through an incision in the femoral artery.

Emboli in popliteal and axillary vessels require removal only when the use of muscles supplied by the vessels remains impossible.

Heparin, intermittent venous compression, antispasmotics, and/or sympathetic blocks should be used as forms of treatment accessory to embolectomy. They should also be used when no embolectomy is done. Their use must be continued for some time.

Attention must be constantly directed to the cardiac disease which in itself may be fatal.

Twenty-four patients with twenty-seven limbs rendered ischemic by embolic occlusion have been studied. Of these limbs, nine were not operated upon. Eighteen limbs were operated upon. In one patient the embolus had moved, and in a second the embolus could not be obtained. Thus, there were sixteen limbs from which an embolus was removed at operation from thirteen patients.

Ten of these emboli were removed within eight hours of their occurrence; all of the patients had satisfactory return of the circulation. Of the remaining six

patients, four were successfully treated (one after twenty-seven hours), one result was doubtful, and one was a failure.

Twelve of the patients studied died. All of these had had emboli removed. Seven patients died within the first few days after the removal of the embolus, apparently from cardiac failure, and all had had successful restoration of the peripheral circulation. Death in four of the remaining five was from causes not related to the heart disease or the embolus and might therefore have been avoided.

AUTHORS.

Barber, R. F., and Madden, J. L.: Resuscitation of the Heart. Am. J. Surg. 64: 151, 1944.

Acute stoppage of the heart is a surgical emergency demanding immediate action if complete recovery is to be obtained. A preconceived plan of therapy avoids delay and confusion.

The percentage of complete recovery in resuscitation of the heart will vary in direct ratio to the time interval between cardiac stoppage and the production of an adequate circulation by massage.

The maintenance of a free and adequate artificial respiratory exchange during the course of resuscitation of the heart is essential.

The cases of cardiac stoppage, capable of complete resuscitation, are those resulting from asphyxia, reflex vagal inhibition, cardiac trauma, cardiac toxins (drugs, anesthetics), acute cardiac dilatation, hemorrhage and vasomotor paralysis with resulting circulatory insufficiency, and electrocution.

The indiscriminate use of the intracardiac injection of epinephrine or other sympathomimetic drugs is condemned.

Sympathomimetic drugs should not be administered during the course of cyclopropane anesthesia.

Procaine hydrochloride (2 per cent) administered prior to, or simultaneous with, the intracardiac injection of epinephrine lessens the possibility of ventricular fibrillation occurring.

The topical application of procaine (5 per cent), metycaine (10 per cent), or cocaine (4 per cent) may also be used to the surface of the heart; the injection of the 2 per cent solution into the chambers of the heart and electrical countershock are the most efficient methods in the treatment of ventricular fibrillation.

The transthoracic approach is the method of choice in the performance of cardiac massage. Exposure of the heart is obtained through a transverse incision in the left third or fourth interspace, the adjacent costal cartilages sectioned, and the corresponding ribs widely retracted.

Manual massage of the heart is the most effective means of initiating cardiac contractions. If uniform success is to be obtained, massage must be performed within three minutes following cessation of the heart beat.

AUTHORS.

Harper, F. R., and Robinson, M. E.: Occlusion of Infected Patent Ductus Arteriosus With Cellophane. Am. J. Surg. 64: 294, 1944.

A case of patent ductus arteriosus in an adult woman, complicated by long standing, severe, subacute, bacterial endocarditis and endarteritis is reported. The patent ductus arteriosus was occluded by ligating it with two silk ligatures and then wrapping cellophane loosely about it. The clinical postoperative course of the patient demonstrated the fact that the cellophane was responsible for the final complete occlusion of the patent ductus arteriosus. For the first two weeks the murmur and symptoms disappeared only to reappear and persist until two and one-half months had elapsed from the time of operation. The murmur and symptoms

then completely disappeared, and the patient has remained entirely well to date, one and one-half years after surgery. The cellophane was thought to be responsible for the final complete and permanent occlusion of the patent ductus arteriosus.

AUTHORS.

Wakerlin, G. E., Johnson, C. A., Moss, W. G., and Goldberg, M. L.: Treatment of Experimental Renal Hypertension With Renal Extracts. J. Pharmacol. & Exper. Therap. **81**: 101, 1944.

The antihypertensive effect of partially purified hog renin in renal hypertensive dogs is definitely superior to highly purified hog renin, suggesting that the active principle is in the nonrenin fraction.

Partially purified heat-inactivated hog renin possesses moderate antihypertensive activity, indicating that the active principle is partially heat-stable.

Partially purified dog renin is not antihypertensive in three times the effective dose of hog kidney, suggesting either that the concentration of the antihypertensive principle is considerably less in dog kidney or that some type of immune response not evoked by homologous renal extract is involved.

Hog liver extract prepared after the manner of partially purified renin was ineffective antihypertensively, suggesting that the antihypertensive potency of our hog renal extracts is not due to a foreign protein effect and that the potency is specific for kidney.

A role for antirenin in the antihypertensive mechanism is largely excluded.

A study of the antihypertensive potency of the nonrenin fraction of partially purified hog renal extract containing renin is well warranted and now under way.

AUTHORS.

Jacobs, J., and Yonkman, F. F.: Sympatholytic Treatment of Experimental Hypertension. J. Lab. & Clin. Med. **29**: 1217, 1944.

Yohimbine hydrochloride, 20 mg. per kilogram of body weight when orally administered, reduces the mean arterial tension of dogs rendered hypertensive by the Page technique of perirenal envelopment.

Reduction of arterial tension was effected in three of four dogs. One was of real significance, another of some, and the third was inconsequential; these appraisals were made after thirty-five, thirty-three, and twenty-three days of medication, respectively. Sustained medication for longer periods would be desirable.

The locus of yohimbine's pharmacologic action in this type of hypertension is probably in the neuromuscular receptors associated with sympathetic vasoconstrictors and is probably antiadrenergic or sympatholytic in nature.

AUTHORS.

Thomas, C. B., and McLean, R. L.: The Effect of Intravenous Injection of Epinephrin and Angiotonin Before and After the Production of Neurogenic Hypertension. Bull. Johns Hopkins Hosp. **75**: 319, 1944.

The pressor responses of unanesthetized dogs to epinephrine and angiotonin were not significantly altered by the induction of neurogenic hypertension.

Angiotonin produces a well-marked cardiac acceleration in the hypertensive animal, whereas it slows the cardiac rate slightly when the dog is in the normal state. Epinephrine has a similar but less marked effect upon the heart rate.

These experiments indicate that while peripheral vasoconstrictor activity may be increased in neurogenic hypertension, vasoconstrictor tone is not sufficiently great to interfere with the action of either sympathicomimetic or humoral vasoconstrictor substances.

It appears that angiotonin stimulates the cardio-accelerator mechanism, but that this effect is normally masked by the moderator reflexes.

AUTHORS.

Book Reviews

ELEMENTS OF ELECTROCARDIOGRAPHIC INTERPRETATION: By Louis N. Katz, M.D., Director of Cardiovascular Research, Michael Reese Hospital, Chicago, and Victor Johnson, Ph.D., M.D., both Professorial Lecturers in Physiology, University of Chicago. University of Chicago Press, Chicago, 1944, ed. 3, 44 pages, 40 illustrations, $1.00.

The purpose of the authors, to provide a booklet "suitable for use by the physician whose specialty lies outside the field of electrocardiography and by the beginning student of cardiac physiology," should be well achieved by this publication. The introductory statements are brief but adequate for a booklet of this character, the plates illustrating electrocardiograms are logically arranged, and the tracings are well reproduced.

The reviewer, however, doubts the wisdom of including, in a work of this type, records whose interpretation is open to any question. The electrocardiogram shown in Plate 9 is certainly one of doubtful character, and, unless students in Chicago are brighter than those elsewhere, one wonders how much this tracing helps to clarify cardiac physiology. Plate 7 should also cause trouble. This electrocardiogram is reproduced as an example of A-V nodal rhythm because of an unusually short P-R interval. The P waves are, however, not inverted, but definitely upright in Leads II and III, which makes it clear that the auricles were not activated from a rhythm center in the A-V node. The record is probably, in the opinion of the reviewer, an example of the so-called Wolff-Parkinson-White syndrome.

Only one definite error was found in the booklet. This occurs in Plate 36, in the first group of tracings. Leads I and II are interchanged, and the latter (Lead I in the figure) is upside down.

The material given in Appendix II, relative to recommended procedure in reading an electrocardiogram, should help those not familiar with interpretation of tracings to approach the records in a logical and systematic fashion.

F. D. JOHNSTON.

American Heart Association, Inc.

1790 Broadway at 58th Street, New York, N. Y.

THE American Heart Association is the only national organization devoted to educational work relating to diseases of the heart. Its activities are under the control and guidance of a Board of Directors composed of thirty eminent physicians who represent every portion of the country.

A central office is maintained for the coordination and distribution of important information. From it there issues a steady stream of books, pamphlets, charts, films, lantern slides, and similar educational material concerned with the recognition, prevention, or treatment of diseases of the heart, which are now the leading cause of death in the United States. The American Heart Journal is under the editorial supervision of the Association.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The income from membership and donations provides the sole financial support of the Association. Lack of adequate funds seriously hampers more intensive educational activity and the support of important investigative work.

Annual membership is $5.00. Journal membership at $11.00 includes a year's subscription to the American Heart Journal (January-December) and annual membership in the Association. The Journal alone is $10.00 per year.

The Association earnestly solicits your support and suggestions for its work. Membership application blanks will be sent on request. Donations will be gratefully received and promptly acknowledged.

**Executive Committee.*